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PRESENT STATUS OF SPECIFIC DRUG TREATMENT OF TUBERCULOSIS

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During the past six years Fitzsimons Army Hospital has participated in the 11 conferences on chemotherapy of tuberculosis sponsored by the Veterans Administration, at which the experiences of 44 hospitals (Veterans Administration, Army, and Navy) have been carefully recorded and analyzed.[1] The latest report of this work on approximately 10,000 cases is now a matter of record. During the period of these studies, the tuberculosis service of this hospital, with an average census of 1,000 patients, has had the opportunity of evaluating antibacterial agents used in the treatment of this disease in adults. The clinical material available has been particularly suitable for pilot studies on the therapeutic effectiveness, bacterial resistance, and toxicity of new drugs and combinations of drugs (table 1). In spite of these experiences and all the excellent reference material available in the literature, it still remains a monumental task to place specific drug therapy of pulmonary tuberculosis in its proper perspective at this time. It should be pointed out also that methods of using chemotherapy have changed each year since the introduction of streptomycin, and there is every reason to believe that new drugs and new concepts in treatments are just beyond the horizon. With such rapid changes it is important that new therapeutic techniques be reviewed at frequent intervals, and consideration given to their practical application under optimal conditions. Every effort must be made to reduce the time interval between fundamental investigation and judicious clinical application. Only in this way will tuberculosis patients benefit promptly from the progress made to date.

FUNDAMENTALS TO CONSIDER IN CHEMOTHERAPY

The plan for integrating chemotherapy with other measures directed toward the arrest or cure of the local disease of the lung is based primarily on an estimation of the clinical pathological findings including: (1) the probable duration of the pulmonary disease (new, old, or mixed lesions), (2) the reversibility of the lesions (resolving or nonresolving infiltrations), (3) the destruction of lung tissue (site, size, and duration of necrotic lesions and cavitation), (4) the extent and localization of the disease (lung, lobe, or segment), and (5) the type and severity of associated lesions of the bronchi and pleural cavity. The effectiveness of new specific therapeutic measures cannot be adequately evaluated without considering the type of lesion under treatment. In planning definitive treatment for active lesions certain generalizations are proper. 1. Patients with exudative disease of recent origin that responds promptly to drug treatment, as evidenced by serial chest roentgenograms, relief of symptoms, and sputum conversion, may be treated successfully with a short course (4 to 8 months) of chemotherapy, whereas patients having new lesions of a caseous pneumonic and cavitary type will usually need a long course (8 to 12 months or more) of drug therapy. 2. Patients with chronic disease who proved to have old irreversible lesions owing to poor response to previous treatment and characteristic clinical and roentgenographic findings are primarily surgical problems. These lesions include chronic fibrocavernous and caseous nodose disease. Chemotherapy should be used as an adjunct to pulmonary resection and thoracoplasty in such cases and continued for a short period (two to four months) after surgery. 3. Patients with mixed new and old pulmonary lesions should receive chemotherapy primarily for the reversible component of the disease and as an adjunct to operative procedures for the irreversible necrotic lesions as suggested above. The duration of drug treatment depends on the type of predominating disease and the plan for chemotherapy in the treatment program. Prolonged drug therapy will usually be required for patients with extensive pulmonary disease of this type.

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Terramycin and viomycin used in these studies were furnished by Charles Pfizer Company, Brooklyn, N. Y., the isonicotinic acid hydrazid by Hoffmann-LaRoche Inc., Nutley, N. J., and the amithiozone by Shenley Laboratories, Inc., New York 1.

1. (*a*) Transactions of the 11th Conference on the Chemotherapy of Tuberculosis, St. Louis, Mo., Veterans Administration Area Office, 1952. (*b*) The Effects of Streptomycin on Tuberculosis in Man: Preliminary Statement, report of the Council on Pharmacy and Chemistry, J. A. M. A. **135**: 634 (Nov. 8) 1947. (*c*) Streptomycin in the Treatment of Tuberculosis: Current Status, report of the Council on Pharmacy and Chemistry, ibid. **138**: 584 (Oct. 23) 1948. (*d*) Current Status of the Chemotherapy of Tuberculosis in Man: A Summary Report, report of the Council on Pharmacy and Chemistry, ibid. **142**: 650 (March 4) 1950. (*e*) Chemotherapy of Tuberculosis in Man: Present Status, report of the Council on Pharmacy and Chemistry, ibid. **147**: 253 (Sept. 15) 1951.

TABLE 1.—*Pilot Study of Drug Regimens for Pulmonary Tuberculosis at Fitzsimons Army Hospital, Among 1,288 Patients, 1946-1952*

Description of Drug Regimen	Year Begun	No. of Cases	Percentage Resistant: Total No. of Patients	Percentage Resistant: Patients with Positive Culture	Comparative Value of Regimens, Comments on Therapeutic Effectiveness, Bacterial Resistance, Drug Toxicity, Patient Acceptance, and Cost *
Daily Dosage Regimens					
Streptomycin 2 gm. daily for 120 days.....	1946	100	64.0	73.5	Daily streptomycin (2 gm. daily 120 days) was the first regimen to be used. It was attended by a high incidence of toxic reaction (especially eighth nerve damage) and bacterial resistance. Except for acute tuberculosis (e. g., miliary) daily streptomycin has been replaced by the intermittent regimen
Streptomycin 1 gm. daily for 120 days.....	1947	37	43.2	66.7	
Streptomycin 1 gm. daily for 42 days.....	1948	133	12.0	18.4	The short regimens (28-42 days) were introduced to decrease drug toxicity and resistance at a time when streptomycin was the only agent available. They served this purpose well and were useful for symptomatic treatment, surgical prophylaxis, and for lesions showing prompt resolution
Streptomycin 1 gm. daily for 28 days.....	1948	117	2.6	3.4	
Streptomycin 0.5 gm. daily for 28 days....	1948	28	0.0	0.0	
P-aminosalicylic acid 12 gm. daily for 120 days.....	1948	37	51.4	59.5	Daily *p*-aminosalicylic acid proved less effective than streptomycin. Drug resistance occurred in more than one-half the cases, but this was shown to be transient. Toxicity reactions were severe in only 5%
Amithiozone 200 mg. daily for 120 days....	1949	42	11.9	14.7	Amithiozone was the least effective of the agents used. Drug toxicity with the 200 mg. dosage proved too great to warrant further use of this regimen
Terramycin 7 gm. daily for 120 days.....	1950	15	6.7	11.1	Terramycin orally proved effective, but the dosage of the pilot study was difficult to administer because of the resulting gastroenteritis. Its present use is limited to combined therapy. The drug cost is high
Isoniazid 150-300 mg. daily for 120 days....	1952	69	10.0	50.0	Isonicotinic acid hydrazid (isoniazid) compares favorably with the therapeutic efficacy of streptomycin and the symptomatic improvement from its use is often more striking. The ease of administration, lack of serious drug toxicity, patient acceptance and low cost are noteworthy. Resistance is a serious problem when the drug is used alone
			Preliminary report at 90 days		
Interrupted Short Course Regimen					
Streptomycin 1 gm. daily for 28 days; repeated after 42 days.....	1948	85	17.1	25.0	This regimen was devised to reduce streptomycin resistance and still provide a relatively long period of drug therapy. It compared well with other 120 day regimens of daily streptomycin and bacterial resistance was greatly reduced. Continuing drugs for entire period of need is now preferred to interrupted courses
Intermittent Dosage Regimens					
Streptomycin 1 gm. twice weekly or once every third day for 120 days.....	1947	50	17.1	25.0	Intermittent streptomycin therapy introduced in 1947 has practically replaced the daily use of this drug for nonmiliary tuberculosis. It gives therapeutic results comparable to daily streptomycin regimens of similar duration without significant toxic reactions to the drug. Bacterial resistance is markedly reduced (none in 42 days; 3.9% at 60 days; 18% at 90 days; 33% at 120 days). No differences between intermittent streptomycin and dihydrostreptomycin regimens were noted. Intermitting drugs reduces cost
Streptomycin 2 gm. twice weekly or once every third day for 120 days.....	1947	50	26.0	34.2	
Dihydrostreptomycin 2 gm. twice weekly or once every third day for 30 days.....	1948	20	0.0	0.0	
Viomycin 2 gm. twice weekly or once every third day for 120 days.....	1951	22	4.5	7.0	Viomycin used intermittently is not very effective from a therapeutic standpoint, and is accompanied by rather high incidence of drug toxicity
Combined Intermittent Regimens					
Streptomycin 2 gm. twice weekly or once every third day.....	1949	95	0.0	0.0	Streptomycin every three days or twice weekly and *p*-aminosalicylic acid daily, has proven effective for periods up to eight months or more, and currently appears to be the best drug regimen of those completely evaluated. It is as effective as the one using both drugs daily, and better than the regimen using both drugs together every three days. Patient acceptance has been good, drug toxicity minimal and the cost most reasonable. Drug resistance has not been encountered in the short term (four months) regimens, but long term (eight months or more) courses of treatment have been difficult to evaluate because of the high rate of sputum conversions during treatment. Of 10 patients with positive cultures at eight months, only 1 revealed organisms resistant to streptomycin and *p*-aminosalicylic acid
P-aminosalicylic acid 12 gm. daily for 120 days.....	....	...	0.0	0.0	
Streptomycin 2 gm. twice weekly or once every third day.....	1949	103	8.7	29.0	
P-aminosalicylic acid 12 gm. twice weekly or once every third day for 120 days....	....	...	0.0	0.0	
Streptomycin 2 gm. twice weekly or once every third day.....	1951	72	1.5	10.0	
P-aminosalicylic acid 12 gm. daily for 240 days.....			Preliminary report at 8 months		
Terramycin 7 gm. twice weekly or once every third day.....	1950	12	0.0	0.0	The combination of terramycin and streptomycin compares favorably with streptomycin and *p*-aminosalicylic acid from the standpoint of therapeutic effectiveness, drug resistance, and toxicity. It is an excellent substitute when *p*-aminosalicylic acid cannot be used because of toxicity. The higher dosage (5 gm. or more) is somewhat difficult to administer because of the resulting gastroenteritis and the cost at present is comparatively high. The smaller terramycin dosage (2 gm.) has not been completely evaluated
Streptomycin 2 gm. twice weekly or once every third day for 120 days.....	....	...	0.0	0.0	
Terramycin 5 gm. daily.....	1951	70	0.0	0.0	
Streptomycin 2 gm. twice weekly or once every third day for 120 days.....		...	0.0	0.0	
Terramycin 2 gm. daily.....	1952	22	Incomplete		
Streptomycin 2 gm. twice weekly or once every third day for 120 days.....		...	....	....	
Viomycin 2 gm. twice weekly or once every third day.....	1951	36	0.0	0.0	Further study on viomycin is required before general use can be advised. Its toxicity limits its application at present, but preliminary studies suggest merit for short courses of intermittent viomycin when combined with streptomycin or *p*-aminosalicylic acid. It is a possible substitute in streptomycin resistance or in toxicity to this drug
Streptomycin 1 gm. twice weekly or once every third day for 120 days.....			2.7	5.5	
Viomycin 2 gm. twice weekly or once every third day.....	1951	21	0.0	0.0	
P-aminosalicylic acid 12 gm. daily for 120 days.....			9.5	18.0	
Amithiozone 100 mg. daily.....	1950	26	0.0	0.0	The toxicity of amithiozone in 100 mg. dosage was slight, but streptomycin resistance makes this combined regimen of little value
Streptomycin 2 gm. twice weekly or once every third day for 120 days.....			20.0	39.0	
Isoniazid 150 mg. daily.....	1952	52	0.0	0.0	Investigation incomplete, but preliminary studies are promising. The cost is low, and isoniazid is more easily administered than *p*-aminosalicylic acid. Drug resistance studies are pending, but the combination isoniazid and streptomycin appears to be effective in delaying resistance to both drugs. The sputum conversion rate is very high, making evaluation difficult
Streptomycin 2 gm. twice weekly or once every third day for 120 days.....		...	0.0	0.0	
			Preliminary report at 90 days		
Isoniazid 300 mg. daily.....	1952	24	Incomplete		
Streptomycin 2 gm. twice weekly or once every third day for 120 days.....		...	....	....	

* Resistance is defined as growth on the control tube equal to the tube containing 10 μg. of streptomycin per milliliter, 10 μg. of *p*-aminosalicylic acid per milliliter, 25 μg. of viomycin per milliliter, 10 μg. of amithiozone per milliliter, 50 μg. of terramycin per milliliter, or 1.0 μg. of isoniazid per milliliter.

There is a continuing realization that drug therapy is only one of the weapons available in the present day treatment of tuberculosis.[2] Clinical investigation indicates that it is best used with rest therapy, preferably in a hospital, and that more frequently than not collapse or other operative procedures will also be required (table 2). It is very important, therefore, to define the missions that drug therapy is intended to accomplish. Chemotherapy in the treatment of pulmonary tuberculosis may be considered definitive (combined with bed rest alone) or adjunctive to other measures (collapse therapy and resection). Occasionally specific drugs are used for symptomatic relief. In rare instances, such as progressive pulmonary lesions of unproven etiology where tuberculosis is strongly suspected, e. g., acute miliary lesions, the use of chemotherapy is justified as a therapeutic trial. In brief, evaluation of the effectiveness of chemotherapeutic agents is more intelligent as well as more practical when made with reference to the particular treatment objective to be achieved.

From experiences at Fitzsimons Army Hospital it may be said that drug therapy when combined with an appropriate period of bed rest is definitive for a considerable number of patients (table 2). Lesions (both new and old) that show prompt resolution following chemotherapy fall in this class. It is recognized that many such lesions, particularly those of minimal extent, can be arrested by bed rest alone if the patient cooperates in treatment. Past experience indicates, however, that the relapse rate over a five year period may be high in patients so treated.[3] The benefits of drug therapy must be evaluated over a longer period to compare with nontreated cases, but the favorable results to date and low incidence of bacterial resistance with the combined drug regimens should make new patients with active pulmonary tuberculosis exceptional if they are not so treated in the future.

TABLE 2.—*Utilization of Chemotherapy in the Treatment of 414 Tuberculosis Patients Discharged from Fitzsimons Army Hospital in 1951 with Maximum Hospital Benefits* *

Treatment	Extent of Tuberculous Lesions					Total Patients †	
	Minimal	Moderately Advanced	Far Advanced	Pleural Effusion	Others	Number	Percentage
Rest therapy only	43	2	0	45	3	93	22
Operations without chemotherapy	..	..	..	..	..	8	2
Temporary collapse	..	3	..	..	..	..	..
Surgery	2	1	..	..	..	..	..
Temporary collapse and surgery	..	2	..	..	..	..	..
Chemotherapy alone (with rest)	40	27	5	21	17	110	27
Operations with chemotherapy	..	..	..	..	..	203	49
Temporary collapse	19	89	22	..	..	..	..
Surgery	6	23	11	5	8	..	..
Temporary collapse and surgery	..	6	14	..	..	..	..
Total	110	153	52	71	28	414	100

* An enumeration of the various forms of treatment used to complete definitive hospital care and successfully carry the patient to the stage of "inactive disease," as defined by 1950 National Tuberculosis Association Diagnostic Standards. The patients were without symptoms, had negative sputum, and the lesions proved stable and noncavitary by serial roentgenograms for at least six months. Treatment was initiated in 1949 and 1950 and reflects the conservative use of drugs of that period.

† This represents approximately one-third of the total tuberculosis patients discharged in 1951. Excluded are the disabled military patients transferred to Veterans Administration Hospitals without completing treatment, deaths, irregular discharges, and inactive patients not requiring therapy.

The phenomenon of resistance of tubercle bacilli to various antibacterial agents is a matter of practical importance. Bacterial resistance may be defined simply as the acquired ability of an organism to multiply or survive in the presence of normally effective concentrations of antimicrobial agents. It is a relative rather than an absolute state. Although the laboratory determination of the presence of resistant organisms is based on arbitrarily selected criteria, there is sufficient correlation with clinical response to justify the use of any reasonable means for preserving the sensitivity of the organism to the drug in question. At the present time this is best achieved by the combined intermittent drug regimens (table 1). Thus, it is important to consider chemotherapy as only one weapon for attacking tuberculosis and to coordinate its use with the rest of the armamentarium in an over-all plan of management in such manner that its effectiveness will not be lost for a crucial period, such as at a time of relapse, or spread after surgery or other complications. Until equally effective antibacterial agents become available, streptomycin resistance must receive special consideration.

COMBINED DRUG REGIMENS

Combined drug regimens have proved to be superior to the administration of single antimicrobial agents in the treatment of tuberculosis.[4] Combinations of drugs and treatment schedules that unite the greatest therapeutic effectiveness with the lowest incidence of drug toxicity and bacterial resistance should be employed. The successful application of such a regimen depends largely on ease of administration, patient acceptance, suitability for long term use, and cost. At the present time the use of intermittent streptomycin and daily *p*-aminosalicylic acid most nearly meets these requirements. This regimen employing streptomycin every third day or twice weekly and *p*-aminosalicylic acid daily appears to be as effective therapeutically as both drugs used together daily [1] or any

2. American Trudeau Society: Current Status of Antimicrobial Therapy in Tuberculosis: Report of the Clinical Subcommittee on Medical Research and Therapy, Am. Rev. Tuberc. **63**: 617, 1951.

3. Mitchell, R. S., and Knudson, J. R.: The Results of the Treatment of Active Minimal Pulmonary Tuberculosis with "Modified Bed Rest": Statistical Analysis of 289 Patients Followed for 7 Years After Discharge from Trudeau Sanatorium, Am. Rev. Tuberc. **61**: 809, 1950.

4. (*a*) American Trudeau Society.[2] (*b*) Tempel, C. W., and others: Combined Intermittent Regimens Employing Streptomycin and Para-Aminosalicylic Acid in the Treatment of Pulmonary Tuberculosis: Comparison with Daily and Intermittent Dosage Schedules, Am. Rev. Tuberc. **63**: 295, 1951. (*c*) Pitts, F. W., and others: Intermittent Viomycin Therapy in Pulmonary Tuberculosis: A Preliminary Report, in Transactions of the 11th Conference on the Chemotherapy of Tuberculosis,[16] p. 270.

other combination of drugs now available when employed for periods of 120 days (table 1). Longer periods (8 to 12 months or more) have not been extensively studied, but little difference in roentgenographic response and sputum conversion between this regimen and the one employing both drugs daily has been demonstrated to date.[1] From the standpoint of patient acceptance, drug toxicity, and cost, the combined intermittent regimen appears to be superior. Bacterial resistance occurring with the long-continued use of these agents has not been thoroughly evaluated, because the high incidence of sputum conversions (approximately 85%) has made it difficult to obtain these studies during treatment.

In seeking other drug combinations to use in the treatment of tuberculosis, it was learned that terramycin could be combined effectively with streptomycin (table 1). It has definitely been established that terramycin in a daily oral dose of 5 gm. combined with 2 gm. of streptomycin every third day will prevent the emergence of streptomycin resistant organism in the 120 day regimen. In a series of 70 patients, 25 had positive sputum cultures on or after 120 days of drug treatment and streptomycin sensitiveness was preserved in each instance.[5] The practical application of this knowledge is at once apparent. Certain patients will find *p*-aminosalicylic acid unacceptable, and terramycin can be substituted, thus preserving the usefulness of streptomycin. In terms of therapeutic effectiveness, terramycin compares favorably with *p*-aminosalicylic acid when used in combination with intermittent streptomycin and no significant toxicity has been noted other than mild gastrointestinal symptoms. Cost and patient acceptance of terramycin in the dosage used does not compare too well with *p*-aminosalicylic acid, but if the lower dosage of terramycin now under study (2 gm. daily) proves effective these disadvantages will be greatly reduced. Serious reaction to *p*-aminosalicylic acid occurred in approximately 5% of our cases; hence, a suitable substitute for this drug to combine with streptomycin must be considered a worthwhile achievement.

Viomycin has not been completely evaluated, but preliminary studies on its use intermittently (every three days) combined with *p*-aminosalicylic acid or streptomycin for 120 days suggests that this drug has definite merit.[4c] Toxic manifestations (pain at site of injection, allergic phenomena, vertigo, renal irritation, and electrolyte changes) were common with this regimen but minor in severity and transient in nature. These troublesome reactions will probably limit the use of this antituberculosis agent to urgent indications where toxicity and bacterial resistance to other drugs may warrant its application for short periods.

The use of amithiozone alone or in combination with streptomycin in the treatment of pulmonary tuberculosis has been disappointing.[6] Whereas, definite therapeutic effect could be attributed to the administration of 200 mg. of amithiozone daily, the benefits were relatively slight and were coupled with a high incidence of clinical (upper gastrointestinal irritation) and laboratory (hepatic and hematopoietic) toxicity. Reduction of the dosage to 100 mg. daily greatly lessened the incidence and severity of toxicity. When 100 mg. of amithiozone daily was combined with 2 gm. of streptomycin every third day no reduction in bacterial resistance to streptomycin was observed. It is, therefore, apparent that streptomycin-amithiozone is inferior to the streptomycin-*p*-aminosalicylic acid regimen of therapy.

One other drug combination under investigation should be mentioned because of current interest in the hydrazine derivatives of isonicotinic acid. Preliminary studies on short courses of isoniazid (150 to 300 mg. per day for the average adult) combined with streptomycin (1 to 2 gm.) every three days are encouraging. This regimen is effective therapeutically, and the combination appears to delay the emergence of bacterial resistance to both drugs. The patient acceptance of isoniazid (isonicotinic acid hydrazid) given orally three times daily is better than that of *p*-aminosalicylic acid in the usual dosage of 4 gm. three times daily. The cost of this new agent is comparably small, and to date little drug toxicity has been encountered. An evaluation of combined streptomycin-isoniazid therapy used over long periods of time will be required, however, before the exact place of this regimen can be assessed accurately. Since resistance to isoniazid used alone does occur, such a combination appears to offer a more promising method of applying this drug in the treatment of tuberculosis.

DURATION OF DRUG TREATMENT

Many problems relative to drug treatment of tuberculosis have been resolved in the past six years. The question of how long to use chemotherapy has not been completely answered, and long-term follow-up studies (five years or more) will be required. The effectiveness of most new drug regimens has been measured in terms of immediate therapeutic benefits rather than in the light of their contribution to the total care of the patient and the successful recovery from tuberculosis. It has been shown that cases of active pulmonary tuberculosis receiving chemotherapy with presently available drugs are definitely benefited to a greater extent by long-term treatment than by the shorter drug regimens and that continuous drug administration is preferable to repeated or interrupted courses.[1] Less apparent, however, is the exact place of the long-term regimen in the plan of treatment of tuberculosis. The answer to this question must await studies on all types of clinical problems, and, since these investigations are not now available, a simple answer cannot be given.

It must be remembered that chemotherapy may be started during any phase of the tuberculous infection, from the onset of the disease to the most chronic stage. The lesions may be of recent origin and responsive to treatment, or they may represent advanced stages of fibrocavernous disease with isolated foci of infection beyond the reach of circulating drugs. It is obvious that in these two extremes, treatment of the first lesion may be concluded successfully with a short regimen of drug treatment, while the latter may not be greatly benefited even though treatment be prolonged for eight or more

5. Miller, F. L., and others: Combined Daily Terramycin and Intermittent Streptomycin in the Treatment of Pulmonary Tuberculosis: A Pilot Study, in Transactions of the 11th Conference on the Chemotherapy of Tuberculosis,[1a] p. 53.

6. O'Dell, E. T., and others: The Administration of Amithiozone Alone and in Combination with Intermittent Streptomycin in Non-Miliary Pulmonary Tuberculosis, in Transactions of the 11th Conference on the Chemotherapy of Tuberculosis,[1a] p. 332.

months. In addition to these local pathological factors, the development of bacterial resistance may also profoundly affect the results of drug therapy.

Most patients with pulmonary tuberculosis, when treated with drugs currently available, show residuals of necrotic disease of some degree. If this is not extensive, prolonged drug treatment may, as in reversible lesions, prove definitive when combined with rest treatment. It is in the group of serious caseous pneumonic lesions, particularly those of far advanced disease, that drug therapy must be considered adjunctive to some operative procedure (table 2). If a cavitary lesion persists it should be closed by some collapse procedure; if this is impossible or undersirable, resectional surgery must be used to conclude treatment successfully. The cavitary lesion usually presents a hazard to the patient from the standpoint of spread and hemorrhage. With the drug treatment now available, many of these patients will continue to have positive sputum following discontinuance of therapy. Whether or not open cavitary lesions can be sterilized by some long-term regimen of drug therapy remains to be proved, but our past experiences with chemotherapy would lead us to believe this may not be possible. From a practical standpoint it should be pointed out that surgery is required to eliminate the destructive cavitary lesion in such patients, and the application of this treatment when its need and feasibility is determined should be made at the earliest moment possible. The localized, encapsulated, necrotic lesions are difficult therapeutic problems to manage. New patients with rather extensive disease may show such favorable healing after prolonged drug therapy that small caseous nodose residuals will be well controlled by this treatment alone. The larger residual caseous pneumonic foci and circumscribed tuberculomas, however, have always been a dangerous source of reactivation of the pulmonary disease. In recent years excisional surgery has often been advised as soon as a reasonable period of stabilization was demonstrated. It seems desirable to continue this practice in order to reduce the period of hospitalization and to encourage the greatest possible patient acceptance for required surgery until some other method of therapy is proved more acceptable. There is a possibility that prolonged drug therapy (8 to 12 months or more) may sterilize nodose noncavitary lesions, making surgery unnecessary or so reduce caseous foci in size that only a wedge or segmental resection is required. This possibility presents new fields of investigation that only years of experience and careful bacteriological studies of the sputum and resected lesions can answer. That resection for such lesions after prolonged drug therapy will be safer and require loss of less pulmonary tissue has been reported by D'Esopo.[7] This problem is undergoing extensive investigation at present. What place this method of treatment will have in our therapeutic armamentarium will probably be determined in part by the practicability of the long-term drug regimens, patient acceptance, toxicity of the drugs available, bacterial resistance, ease of administration, the number of new effective drugs discovered, and cost of the agents used. It seems reasonable to predict, as these handicaps to chemotherapy are overcome, that treatment will be continued to the stage of "inactive disease" or some similar period of recovery found to give the best results. Present experience leads us to believe that most patients seriously in need of chemotherapy for active pulmonary tuberculosis will in the future be offered some form of continuous long-term drug treatment.

SUMMARY

1. In reviewing the present status of the specific drug treatment of pulmonary tuberculosis, the importance of adopting new drugs and therapeutic regimens as soon as fundamental investigation establishes their value has been stressed.

2. There is a growing realization that chemotherapy of pulmonary tuberculosis is only one aspect of the definitive treatment of this serious disease and that the application of modern methods of management requires a broad understanding of all phases of the problem of caring for tuberculosis patients.

3. The plan for integrating chemotherapy with other measures directed toward the arrest or "cure" of the local tuberculous process in the lungs requires a careful evaluation of the individual case, including an estimation of the type of disease present in terms of duration, extent, pathological type, destructiveness, and the potentiality to respond to treatment. The usefulness and effectiveness of chemotherapy cannot be evaluated without paying heed to these factors. Lesions of recent origin showing prompt resolution may be treated successfully with a short course (4 to 8 months) of chemotherapy, whereas new lesions with serious caseous pneumonic, necrotic, or cavitary components will usually be deserving of a long course (8 to 12 months or more) of drug treatment. Old irreversible lesions responding poorly to treatment are primarily surgical problems. The question of how long to use chemotherapy for the various forms of pulmonary tuberculosis has not been completely evaluated to date.

4. Combinations of drugs and treatment schedules that combine maximal therapeutic effectiveness with minimal drug toxicity and bacterial resistance should be employed. The ideal drug regimen should be easy to administer over prolonged periods and of reasonable cost. Of the specific antituberculous drugs properly investigated and available for general use early in 1952, the regimen of choice is streptomycin intramuscularly every three days or twice weekly, combined with oral *p*-aminosalicylic acid daily. Terramycin has been found to be useful as a substitute for *p*-aminosalicylic acid in those instances in which toxic manifestations to the latter drug required this. Like *p*-aminosalicylic acid it delays the emergence of streptomycin-resistant organisms. Viomycin is still under investigation, but preliminary studies on its use intermittently (every three days) combined with *p*-aminosalicylic acid or streptomycin suggest that this drug has definite merit. Amithiozone possesses a high degree of toxicity, which is coupled with low therapeutic effectiveness. The latest drug under clinical investigation in the treatment of tuberculosis is isoniazid (isonicotinic acid hydrazid). Preliminary reports are very encouraging, but the therapeutic effectiveness, toxicity, and bacterial resistance to this drug when used alone and in combination with other agents for long periods has not

7. D'Esopo, N., and others: The Bacteriology of Resected Lesions During Chemotherapy, in Transactions of the 11th Conference on the Chemotherapy of Tuberculosis,[1a] p. 230.

been completely evaluated. Resistance to isoniazid used alone does occur; hence, some combination with other drugs will be required to preserve its usefulness.

CONCLUSIONS

Chemotherapy in tuberculosis should be considered along with the rest regimen and operative procedures integrated into a coordinated plan of total care and offered as promptly and energetically as response to treatment warrants. Consideration must be given to the application of broad principles of management to the individual types of pulmonary tuberculosis, and treatment carried out as individually required for each patient on the basis of sound clinical principles.

It must be remembered that tuberculosis is a serious contagious disease and prone to relapse. Amberson [8] said, when considering the need for antibacterial agents that will completely destroy the tubercle bacillus in the human body, "As the historic consistency of the bacillus is a warrant of its future predictability, there is hope that eventually its inroads may be effectively blocked, at least at those points where it operates stubbornly in only one or a few ways. This is not to say that the tubercle bacillus will ever be annihilated. An assumption or even a hope of that sort would have to go begging for scientific support. Through the eons of evolution this mycobacterium—possibly one among many—has adapted itself almost perfectly as an obligatory parasite, excelling in this way even the staphylococcus and the colon bacillus. Its inroads may be checked and its territory confined, but to look for its extermination would be to ignore its tenacity of life and the consistency of its behavior. It would be wiser by far to plan for its long survival, to assume its undeviating parasitism, to anticipate its readiness to destroy the defenseless and, hence, to maintain defenses permanently and well." As applied to chemotherapy this may be interpreted to mean that "wonder drugs" should not replace common sense in the control and treatment of tuberculosis.

8. Amberson: Preface, in Willis, H. S. K., and Cummings, M. M.: Diagnostic and Experimental Methods in Tuberculosis, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1952.

CURRENT STATUS OF ANTIMICROBIAL THERAPY IN TUBERCULOSIS

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Specific antimicrobial therapy has been accepted generally as of great value in the treatment of tuberculosis. Intensive clinical investigations, particularly those sponsored by the Veterans Administration-Army-Navy Conference, are constantly adding to our knowledge in this field. For this reason, it is necessary to reconsider and revise our regimens of treatment at frequent intervals. In spite of the progress that has been made in the treatment of tuberculosis, there is no evidence that any drug or combination of drugs is sufficiently potent so that other forms of treatment, such as rest, collapse therapy, and excision, may be dispensed with. Consequently, it should be emphasized that from the beginning specific antimicrobial therapy should be carefully coordinated with other forms of treatment. In most instances this is best done in a tuberculosis hospital or in the tuberculosis division of a general hospital. Whereas the discovery of penicillin simplified the treatment of pneumococcic pneumonia and certain other infectious diseases, the discovery of potent antituberculosis drugs has made the treatment of this disease more complex and increased the need for thoroughly trained phthisiologists.

INDICATIONS FOR ANTIMICROBIAL THERAPY

In the early days of the use of streptomycin, the frequency of toxic reactions and the emergence of drug resistant strains of tubercle bacilli led to the advice that streptomycin be given to patients with tuberculosis only if other forms of treatment were unsatisfactory.[1] Subsequent developments have decreased the frequency of these complications sufficiently, so that most clinicians now agree that antimicrobial therapy should be used more liberally.[2] In fact, it seems to me that specific antimicrobial therapy should be used in any case of active tuberculosis with reversible disease or reversible symptoms, unless there is some specific contraindication. This includes patients with active minimal pulmonary lesions, tuberculous pleurisy with effusion, advanced tuberculosis of the lungs, genitourinary tract, skeletal system, lymph nodes, bronchi, larynx, and intestines, and the rarer manifestations of the disease, such as tuberculosis of the peritoneum, pericardium, skin, middle ear, and eye. Obviously, antimicrobial therapy is mandatory for such serious forms of the disease as miliary tuberculosis and tuberculous meningitis.

Primary tuberculosis presents a more controversial problem. Most clinicians do not recommend routine antimicrobial therapy of uncomplicated primary tuberculosis in children, but Lincoln's report [3] that 23.9% of 622 patients who had primary tuberculosis as children died subsequently of tuberculosis suggests that the older forms of treatment of primary tuberculosis are not completely satisfactory. It seems desirable for someone to study this problem by treating half of the patients of a group with antimicrobial agents and then following the whole group long enough to learn whether the treated patients fare better than the control patients. Certainly, any evidence of progressive primary disease would call for intensive antimicrobial therapy. Postoperative complications due to tuberculosis may be prevented by the administration of antimicrobial agents at the time of the surgical treatment of tuberculosis, particularly when

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From the Division of Medicine, Mayo Clinic.

Read before the Section on Internal Medicine at the 101st Annual Session of the American Medical Association, Chicago, June 10, 1952.

1. American Trudeau Society: Streptomycin in the Treatment of Tuberculosis: Report of Clinical Subcommittee, Am. Rev. Tuberc. **59**: 106-110 (Jan.) 1949.

2. American Trudeau Society: Current Status of Antimicrobial Therapy in Tuberculosis: Report of Clinical Subcommittee of Committee on Medical Research and Therapy, Am. Rev. Tuberc. **63**: 617-624 (May) 1951.

3. Lincoln, E. M.: The Value of Follow-Up Studies of Children with Primary Tuberculosis, Am. Rev. Tuberc. **64**: 499-507 (Nov.) 1951.

tuberculous tissue is transected. For this reason, the two forms of therapy should be carefully coordinated so that the surgical procedures will be performed while the tubercle bacilli are still sensitive to the antimicrobial agents.

CHOICE OF DRUGS

Streptomycin and Dihydrostreptomycin.—These drugs remain the most potent agents available for the treatment of tuberculosis. Neither drug is clearly superior to the other in therapeutic efficacy or in freedom from toxic reactions in the usual dose. Unfortunately, strains of tubercle bacilli resistant to one of these drugs are always equally resistant to the other. Clinical studies are now in progress that may eventually settle the problem of which of these drugs is better. It is now agreed generally that the intramuscular administration of 1 gm. of streptomycin or dihydrostreptomycin to the average adult with tuberculosis two to three times each week is as effective therapeutically as daily administration of the same dose. As this interrupted regimen is cheaper and produces fewer toxic reactions and fewer drug resistant strains of tubercle bacilli, it is the regimen of choice. Daily therapy is probably advisable for more serious forms of tuberculosis, such as tuberculous pneumonia, miliary tuberculosis, and tuberculous meningitis, but there is no evidence to prove this. Neither is there any convincing evidence that the intrathecal administration of streptomycin has any effect on the prognosis in tuberculous meningitis. When given intrathecally, the usual dosage is 50 mg. every other day.

As the streptomycin drugs are excreted through the kidneys, impairment of renal function may result in the cumulation of toxic concentrations of the drug in the body. For this reason, the renal function should be measured before treatment, and if it is impaired the dose of streptomycin should be adjusted. The commonest toxic reactions to streptomycin drugs are allergic reactions, that is, drug fever, dermatitis, and neurological reactions, including auditory and vestibular damage. The allergic reactions are commoner when streptomycin is used than when dihydrostreptomycin is used and may be controlled by desensitization of the patient or by changing to dihydrostreptomycin. Neurotoxic reactions may be related to the cumulation of toxic concentrations of streptomycin in the body owing to the administration of large daily doses of the drug or to impairment of renal function. Decreasing the dose or discontinuing the administration of the drug may prevent a serious neurotoxic reaction. For this reason, the auditory and vestibular function should be measured before treatment and every two to three months during treatment, so that neurotoxic changes may be detected early. Occasionally, the character of the disease may warrant continued administration of the drug in spite of a neurotoxic reaction. In such cases, the predilection of streptomycin for causing vestibular damage and of dihydrostreptomycin for causing deafness may aid the clinician in his choice.

p-Aminosalicylic Acid.—After the streptomycin drugs, *p*-aminosalicylic acid is the next most widely used drug in the treatment of tuberculosis. It is weakly effective against the disease when used alone and is usually given orally along with streptomycin to prevent or delay the emergence of strains of tubercle bacilli resistant to streptomycin. Administration of this drug on only two or three days each week has proved unsatisfactory,[4] so daily treatment is advisable. The optimal regimen is unknown, but the generally recommended daily dose is 12 gm. divided into three or four doses. Experimental tuberculosis in guinea pigs responds satisfactorily to a single daily dose of *p*-aminosalicylic acid,[5] and such a regimen should be studied clinically. The sodium salt of *p*-aminosalicylic acid causes fewer gastrointestinal reactions than the free acid and is the most commonly used form of the drug, the daily dose being adjusted to equal 12 gm. of *p*-aminosalicylic acid.

p-Aminosalicylic acid may be given parenterally, and for this route a lyophilized preparation of the sodium salt is used.[6] By this route, large doses, up to 30 gm. of *p*-aminosalicylic acid per day, may be given without the production of gastrointestinal symptoms. Moeschlin and Löffler [7] have reported this dose of *p*-aminosalicylic acid combined with streptomycin to be very efficacious in the treatment of tuberculous meningitis. Serious toxic reactions to *p*-aminosalicylic acid are rare. Drug fever and dermatitis have occurred and are usually controlled by desensitization of the patient with increasing doses of *p*-aminosalicylic acid. Occasionally gastrointestinal irritation is so severe that administration of the drug must be stopped. Boger and Fitzpatrick [8] have reported that benemid® (probenecid, or *p*[di-*n*-propylsulfamyl]benzoic acid) impairs the metabolism and excretion of *p*-aminosalicylic acid, so that a daily dose of 8 gm. of *p*-aminosalicylic acid with probenecid is equal to a daily dose of 12 gm. of *p*-aminosalicylic acid without probenecid. Others have confirmed this report, and further clinical study of this combination seems advisable.

Nicotinic Acid Derivatives.—Pyrazinamide, isoniazid (isonicotinic acid hydrazid), and iproniazid (1-isonicotinyl-2-isopropyl hydrazine) recently have been reported to be potent agents against the tubercle bacillus in vitro and against experimental tuberculosis in mice, guinea pigs, and rabbits.[9] Preliminary clinical reports [10] indicate

4. Hughes, F. J.; Mardis, R. E.; Dye, W. E., and Tempel, C. W.: Combined Intermittent Regimens in the Treatment of Non-Miliary Pulmonary Tuberculosis: A Comparison of SM Every Third Day and PAS Daily with SM Every Third Day and PAS Every Third Day, in Transactions of the 10th Conference on the Chemotherapy of Tuberculosis (Streptomycin Conference), Atlanta, Ga., Veterans Administration Office, 1951, vol. 10, pp. 67-76.

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8. Boger, W. P., and Fitzpatrick, F.: "Benemid" as an Adjunct to Para-Aminosalicylic Acid Therapy, Tuberculology **12**: 162-170 (Aug.) 1951.

9. Bernstein, J.; Lott, W. A.; Steinberg, B. A., and Yale, H. L.: Chemotherapy of Experimental Tuberculosis: Isonicotinic Acid Hydrazide (Nydrazid) and Related Compounds, Am. Rev. Tuberc. **65**: 357-364 (April) 1952. Steenken, W., Jr., and Wolinsky, E.: Antituberculous Properties of Hydrazines of Isonicotinic Acid (Rimifon, Marsilid), ibid. **65**: 365-375 (April) 1952.

10. Robitzek, E. H., and Selikoff, I. J.: Hydrazine Derivatives of Isonicotinic Acid (Rimifon, Marsilid) in the Treatment of Active Progressive Caseous-Pneumonic Tuberculosis: A Preliminary Report, Am. Rev. Tuberc. **65**: 402-428 (April) 1952. Elmendorf, D. F., Jr.; Cawthon, W. U.; Muschenheim, C., and McDermott, W.: The Absorption, Distribution, Excretion, and Short-Term Toxicity of Isonicotinic Acid Hydrazide (Nydrazid) in Man, ibid. **65**: 429-442 (April) 1952.

that these drugs are effective in the treatment of patients with tuberculosis. They seem to be relatively nontoxic in therapeutically effective doses and can be given either orally or parenterally. Further clinical investigations are needed to determine which of these drugs is best and its exact place in the treatment of tuberculosis. At the present moment isoniazid seems to be the drug of choice. Strains of tubercle bacilli have already developed resistance to this drug so that it seems likely that isoniazid will have to be used in combination with streptomycin or *p*-aminosalicyclic acid, or possibly the concurrent administration of all three drugs will prove to be the most therapeutically effective regimen.

Other Drugs.—Two drugs that have shown promise in experimental studies and in preliminary clinical studies are terramycin and viomycin; however, neither of these drugs can be recommended for general use at this time. The thiosemicarbazones, particularly amithiozone, have been studied intensively and are effective especially in the treatment of tuberculosis of the mucous membranes; however, hepatotoxic and hematotoxic reactions have been so common that these drugs should be used only when other antituberculosis drugs have failed and then only with great caution. The sulfones, neomycin, and mycomycin have been tried and found ineffective or toxic and need no further consideration in this report.

IMPORTANCE OF COMBINED THERAPY

The frequent emergence of drug resistant strains of tubercle bacilli is a serious complication of the administration of streptomycin alone. This same phenomenon has been found to occur whenever a potent antituberculosis drug is given alone. Fortunately, resistance is a drug specific characteristic and a strain of tubercle bacilli resistant to one drug is usually sensitive to another; however, tubercle bacilli resistant to both streptomycin and *p*-aminosalicylic acid have been obtained when *p*-aminosalicylic acid has been given to a patient with tubercle bacilli that were resistant to streptomycin. The concurrent administration of two or more of these drugs has been shown to delay or even prevent the emergence of drug resistant strains of tubercle bacilli. For this reason, it seems unwise ever to give a single antituberculosis drug to a tuberculous patient unless there is some compelling reason for such action.

The exact degree of drug resistance that renders further therapy with that drug useless is not known for any of the antituberculosis drugs. Resistance to streptomycin has been studied more intensively than resistance to any other drug, and it is now known that further streptomycin therapy is still of value when the tubercle bacilli are completely resistant to 10 μg. of streptomycin per cubic centimeter of culture medium and even when the bacilli are partially resistant to 100 μg. of streptomycin per cubic centimeter of culture medium.

The optimal duration of treatment with the antituberculosis drugs available today is unknown. Streptomycin given alone has usually been effective for only 60 to 120 days, owing to the frequent emergence of streptomycin resistant strains of tubercle bacilli. The administration of streptomycin on only two or three days each week combined with daily administration of *p*-aminosalicylic acid has markedly delayed the emergence of strains of tubercle bacilli resistant to streptomycin and increased the period of therapeutic effectiveness. Consequently, the effect of treatment with these two agents for periods up to one year and even longer is being studied. Preliminary reports indicate that treatment for the longer periods is significantly more effective than that for shorter periods. These data suggest that the minimal period of treatment for any patient is 6 to 8 months and that this should be extended to from 12 to 24 months in the more serious manifestations of tuberculosis.

SUMMARY

Antimicrobial agents have become indispensable in the treatment of tuberculosis but should be combined with other forms of treatment, such as rest, collapse therapy, and surgical procedures. Antimicrobial therapy is indicated in all cases of active tuberculosis with reversible disease or symptoms.

The best regimen available today for most patients with tuberculosis is 1 gm. of streptomycin or dihydrostreptomycin given intramuscularly two or three times each week plus 12 gm. of *p*-aminosalicylic acid given orally each day.

The optimal duration of therapy with a streptomycin drug and *p*-aminosalicylic acid in combination is not known. At least 6 to 8 months is advisable for all patients and 12 to 24 months for those with more serious disease.

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The Artificial Kidney.—Within the last few years . . . the use of the so-called "artificial kidney" has increased, and its potentialities as well as its limitations have begun to be realized through larger experience. All of these devices . . . function by causing blood from the animal or patient to course through a cellophane tube or between two cellophane sheets. On either side of the cellophane membrane is opposed a dialyzing bath appropriately formed with regard to its electrolyte and osmolar composition. The cellophane membrane is impermeable to molecules with molecular weights of about 20,000 or over so that the serum proteins are retained and larger amino acids pass slowly, if at all. The smaller molecules including metabolites such as urea, phosphates, sulfate, and potassium diffuse easily through the pores of the cellophane and are removed in the rinsing fluid on the other side. Since the concentration of essential electrolytes in the bath is such as to affect no gradient for these across the membrane, there is no net exchange of these substances and thus no change in the serum concentration. It is possible, however, if one wishes to remove potassium, for instance, to eliminate potassium from the dialyzing bath. . . . On the other hand, if the plasma level of sodium is lower than that in the bath fluid, an influx of sodium into the plasma occurs from the bath as a result of this gradient, and this may occur at the same time that potassium is moving in the opposite direction. The fact that such transfers may be effected across an inert membrane and in accord with relatively simple physical chemical laws gives the artificial kidney an advantage over techniques such as intestinal irrigation in which the membrane involved is governed by more complicated metabolic processes involving selective resorption and transfer. . . . Not the least important responsibility of the physician in the use of the artificial kidney for the treatment of chronic uremia is the necessity for carefully explaining to the patient's family the limitations of the procedure and exactly what is to be expected. A tragic by-product of this technique is the raising of false hopes with subsequent disappointment and disillusionment.—John P. Merrill, The Use of the Artificial Kidney in the Treatment of Uremia, *Bulletin of The New York Academy of Medicine*, August, 1952.

INDUSTRIAL MEDICAL ASPECTS OF CHEST DISEASES OF OCCUPATIONAL ORIGIN

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This discussion is concerned with the management of that patient or groups of patients on whom the label of a pulmonary dust disease has been placed either by the family physician or by a consulting chest specialist. From the narrower viewpoint, it is the classification that has been applied to those persons who are referred to our office for evaluation and treatment. Such patients may or may not have true pulmonary fibrosis, but they always present symptoms that, in one fashion or another, are referable to pulmonary disability. These considerations make it important that all the factors that have contributed to the disease process and the subsequent disability be studied as objectively as possible with whatever tools and disciplines are available.

DIAGNOSTIC CONSIDERATIONS

The diagnosis of pulmonary dust disease, as of any other occupational disease, implies that injury has been sustained in and because of the working environment and that financial compensation is forthcoming for the disability so produced. Almost without exception, the patient himself will be convinced of the cause of his difficulty and will claim compensation. Ready agreement on the part of the physician with the diagnosis and prognosis that have been arrived at by the patient himself will lead to economic and sociologic complications that will render logical treatment, physical improvement, and return of the patient to a productive capacity extremely difficult.

It cannot be denied that much confusion exists because of the lack of generally acceptable criteria for diagnosis. Some physicians rely entirely upon the chest roentgenogram for the diagnosis and prognosis, while to others the mere fact that the patient says that he has been exposed to a certain material is adequate justification for a diagnosis of occupational pulmonary disease.

If such empiricism is injurious to the patient, what then are the criteria that make possible a diagnosis such as silicosis? It is doubtful that the fundamental factors enumerated by Gardner [1] as contributing to the diagnosis of silicosis have yet been improved upon. The first is evidence of changes in the lungs demonstrated in roentgenograms and manifested anatomically by the formation of sharply defined fibrous nodules, not over 4 to 6 mm. in diameter, which in most cases are uniformly distributed throughout all portions of the lungs. The second is a history of exposure to silica dust, adequate to produce such disease. The third factor is the evidence of infection and disability obtained by examination. If silicosis is to be considered purely an anatomic diagnosis, then the first two of these factors by themselves are adequate, but in such a diagnosis there cannot be any implication of disability. It must not be forgotten, however, that such a technical limitation of the diagnosis has no meaning for the patient to whom the word silicosis is synonymous with serious disablement. The layman cannot be aware of the fact that uncomplicated silicosis rarely produces enough disability to prevent pursuit of his usual occupation. Therefore, a satisfactory diagnosis is possible only when all three factors are applicable and interrelated.

In the absence of specific roentgenographic evidence of nodulation, one might expect an unwillingness or at least some reluctance on the part of the physician to state definitely that the patient has silicosis. Unfortunately, even this lack of evidence does not act to assure an objective evaluation of the individual patient. The presence of reticulation alone, in the absence of other criteria, is now accepted by many physicians as being of etiological significance and of prognostic value. This roentgenographic reticulation has also been described as "granular silicosis" and "atypical silicosis," with apparently little consideration for the anatomic features that may produce this radiographic phenomenon. Reticulation has been described [1a] as "a pulmonary reaction characterized anatomically by accumulations of dust-filled phagocytes and proliferation of cellular connective tissue in the larger septa and trunks, and roentgenographically by exaggeration of the linear shadows chiefly cast by the blood vessels and which may be due to a variety of causes." Although such appearances may be a manifestation of beginning silicosis, in which case it may later progress to the stage of nodulation, they may also be caused by the inhalation of nonsiliceous dusts that produce only linear reactions without further progression. In any event, the roentgenographic appearance of linear exaggeration, when it is due to the inhalation of silica dust, is rarely associated with disability.

In considering a diagnosis of occupational chest disease, familiarity with the patient's previous working environment should be of prime importance to the examining physician. Such firsthand knowledge is rarely possessed even by those physicians whose time is devoted largely to industrial practice. A carefully taken occupational history will, however, be of the greatest aid in the absence of personal observation. To be of any value, such a history must be taken with the purpose of understanding and evaluating the environment in which the worker spends approximately one-third of his time. Etiologically, it may be of greater significance than either the family history or the social history, both of which are frequently reported at length. If the patient has been a miner, one should know the type of mines in which he has worked and the exact type of work that he has done. Was he a driller, a mule driver, a timberer, or a mucker? Did he spend much time at the working face of the mine,

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Because of space limitations, some of the bibliographic references have been omitted from THE JOURNAL and will appear in the author's reprints.

Read before Joint Meeting of the Section on Military Medicine, the Section on Preventive and Industrial Medicine and Public Health, and the Section on Radiology at the 101st Annual Session of the American Medical Association, Chicago, June 10, 1952.

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did he drive a raise, or did he even work underground? It is not uncommon for a diagnosis of silicosis to be made for patients who call themselves miners but have never been exposed to dust of any kind. If the patient has been a worker in any nominally dusty industry, it is well to ascertain specifically whether exposure to appreciable amounts of dusts occurred. Although many of the patient's statements will be influenced by his opinions, an amazing amount of useful information will be gained by detailed questioning concerning the person's actual work.

Even when a history indicative of serious dust exposure is obtained, one must not forget that the industrial worker is not exempt from diseases of nonoccupational origin, particularly when the roentgenographic evidence of disease is not consistent with the history of exposure to harmful dust. Pulmonary fibrosis is not a specific entity, and, in addition to causation by industrially generated dust, it may be produced by other agents and especially by micro-organisms. There are many [2] reports of pulmonary fibrosis of indeterminate cause, even after careful clinical and postmortem study.

DISABILITY DETERMINATIONS

Having established the diagnosis of occupational pulmonary disease, the physician must be concerned with determining the amount of disability and the physiological reason for its presence. Pulmonary function studies have been considered to be ideal in the evaluation of disability, and they have indeed contributed materially to our information concerning pulmonary disability. In the present state of our knowledge, these cannot, however, be considered the final answer to the study of disability. In addition to general lack of availability of pulmonary function studies, the very wide range of the values that are regarded as normal makes it necessary that the results of such studies be interpreted critically and that they be correlated with clinical findings. Since they are perhaps of the greatest value in determining the patient's ability to do work rather than the loss of ability he has sustained, it would probably be more realistic to evaluate the patient from the former point of view. In general, however, any objective determinations of capacity for effort that can be carried out on patients with pulmonary disease will contribute tremendously to our clinical evaluation.

Clinical observation of the patient from the point of view of effort will provide much valuable information that can be correlated with other findings. Does the patient wheeze? Does he have acute attacks of dyspnea? Can he carry on a conversation effortlessly, or does he speak gaspingly? Does he cough frequently during effort? Can he walk several hundred feet on a level surface (with the examiner) and carry on a conversation at the same time? How much distress is produced by walking up one flight of stairs? These and many other types of simple observations can be made by any physician and can be employed in arriving at fairly reliable estimates of pulmonary disability, particularly after a little experience. Fluoroscopy with observation of the motion and position of the diaphragms, the ventilatory ability, and the movement, if any, of the mediastinum will also be of aid when compared with the clinical findings.

Disability may be produced by many physiological factors, but bronchitis and bronchiolitis, which are due to infection, are the usual complications that modify the clinical course of many chronic chest diseases and contribute to the loss of physical ability. Accompanying this infection and as a consequence of it, bronchiolar edema provides a serious impediment to respiratory function. Neither of these conditions can be identified radiologically, but both are obvious in the clinical examination. So much blocking of the airways may have occurred that the patient is frequently thought to have true bronchial asthma. Indeed, some authors [3] have suggested a definite allergenic factor in silicosis based on the facts that colloidal silica has a bronchoconstrictor [4] effect, that epinephrine clinically relieves dyspnea and bronchospasm in silicotics, and that histamine clinically causes dyspnea and wheezing in silicotics.[3] Our own observations suggest that freshly inhaled silica does produce the above described bronchospasm but that antihistamine therapy is of no value in the therapy of this condition.

It has been stated [5] that impairment of the physiological defenses of the bronchopulmonary system seems to explain in part the susceptibility of many silicotic patients to severe respiratory infections and that even if such patients recover from pneumonia such an episode may be followed by a decided increase in persistent respiratory disability. Our own observations and those of others [6] indicate that the increased disability is probably due to the fact that all infection has not been removed and that the underlying causes of physiological dysfunction are still present. In either case, it is essential that the patient with chronic pulmonary disease be protected as early and as adequately as possible against respiratory infection of any type. Thus, when antibiotic or other antibacterial therapy is instituted, adequate dosages must be maintained until the physician is assured that the infection has been eliminated.

The presence of other infectious processes that may contribute to the pulmonary infection must also be noted. A very large number of these patients have pyorrhea and severe dental caries. If pharyngeal reflexes are absent or impaired frequently, as has been noted,[5] the likelihood of the aspiration of infectious material is apparent. In addition, the presence of such foci of infection is a serious part of the entire disease process present in these patients. The generally poor state of nutrition that is observed especially in chest patients of advanced age is difficult to improve in the absence of good oral hygiene and of adequate numbers of opposing teeth. Subclinical avitaminosis and general malnutrition are common observations. General physical improvement frequently follows the administration of vitamin and protein supplements, and the ability to ingest an adequate diet results in rapid weight gain. Although emaciation is seen in many of these patients, obesity is not uncommon among those

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who have not worked for several years. Once the patient has been retired, he overeats, becomes indolent, and greatly limits his physical activity. This combination further serves to increase his disability, and the patient is always surprised when the loss of a few pounds of weight results in less dyspnea and fatigue on effort.

In addition to infection, emphysema must be considered as the commonest complication and disabling factor, particularly in advanced silicosis. Pneumoperitoneum has not been shown to be of value in the treatment of silicotic emphysema, but reeducation in breathing does result in improvement in most instances. Any type of unusual complication may be found in the occasional case, but the average case is uncomplicated. Although bronchiectasis is commonly reported, it is not often verified. Whenever a suppurative pneumonic process occurs, however, bronchiectasis can and does follow. Such a complication is a difficult hurdle for any patient and furnishes a particularly poor prognosis in the case of the person with silicosis.

MEDICAL MANAGEMENT

To combat infection and bronchiolar obstruction, the use of bronchodilator agents and intermittent positive pressure breathing [6a] has proved most effective. The bronchodilator drugs are disseminated as aerosols by means of a nebulizer that is combined with the positive pressure breathing respirator. By this method the aerosol becomes more uniformly distributed throughout the lung, and mucous secretions blocking the bronchi and smaller air passages are loosened. With promotion of better drainage, the aerosol becomes more effective and gaseous exchange is improved. Many data [6b] have been accumulated to show that this method of treatment results in increased oxygen saturation of the arterial blood and in decrease in the mean oxygen pressure gradient from alveoli to arterial blood.

The improvement produced by the intensive therapy outlined above can be maintained for unlimited periods of time if proper management of the patient is continued. He must be encouraged to return to some type of productive work and to continue special breathing exercises [7] designed to promote the fullest use of the remaining lung capacity. The finding of employment that is suitable and not beyond the capacity of men afflicted with chronic pulmonary disease is absolutely essential to their future physical welfare, because lack of useful occupation almost always results in both physical and mental deterioration. Indifference to this important facet of the patient's welfare will not yield persistent beneficial results.

Perhaps the greatest difficulty in returning the patient to work will be the problem of motivation. It has been stated repeatedly that incentive cannot be measured, nor can it be provided when entirely absent. My own experience shows that when the patient and his environment are studied closely, a reasonable estimate of motivation can be obtained and the patient can be made to understand why he should return to work. Of all the factors that are important in the management of chronic pulmonary disease, this is perhaps the most difficult and yet the most essential. For some persons, many hours of discussion and study are required; in still other cases, psychiatric guidance may be needed. Only in the exceptional case has this type of endeavor proved fruitless. Regardless of method, however, experience shows that intelligent appraisal of individual problems will produce favorable results in terms of both improvement of the disease and productivity of the patient.

As a direct result of these factors, unusual care in the planning of the medical management of the patient must be taken from the time that he first presents himself to a physician. A careless or inaccurate diagnosis or a misunderstanding of the words occupational or industrial at the time of this visit may set in motion a chain of events, the effects of which will increase by geometric rather than by merely arithmetical progression. To the patient, such terms as silicosis, anthracosis, and asbestosis do not represent fibrosis, emphysema, or any other anatomic deviation; to him they connote "miner's consumption" or cancer, diseases from which his relatives or friends have died at an early age. Implicit in his concept is the fear that he too is destined to suffer the effects of lingering disease. Unless told firmly to the contrary, he will be convinced that he has active tuberculosis.

The first thought that suggests itself to the patient is that he must never again return to work. All too often this suggestion is confirmed by the physician. In instances in which advanced disease is present and the patient is suffering from definite respiratory difficulty, this admonition is essential. Frequently, however, these warnings are given to patients whose degree of disability is negligible, whose history of exposure has been extremely brief, and who in fact are not suffering from the effects of dust inhalation. It will be suggested that such instances of professional resort to melodrama are rare or even that they derive from the patient's misrepresentation or misinterpretation of statements made by his physician. Let me hasten to add, however, that these impressions have not been formed from what the patient says the physician told him; rather, they stem from reading the medical reports filed by the physicians who refer the patients to us. All too frequently we read, "This patient must never be exposed to dust again"; or "This man can never do work of any kind"; or, from a recent report, "This patient must never work again, nor must he talk." The last statement was made concerning a patient whose chest roentgenogram showed no definite abnormality, who was able to walk up two flights of stairs at a moderate rate without dyspnea, but who was firmly convinced that he had not long to live. Such remarkable concern over a disease process and equally unusual indifference toward a patient in whom the disease is reputed to exist serve no useful therapeutic function; instead, they usually militate against effective treatment and eventual improvement.

As one sees and examines numbers of persons with respiratory complaints, the truth of Parkinson's [8] statement becomes more apparent: "We come to perceive that it is the individual with whom we must deal, and that his disease is no more than a circumstance. The bulk of our practice consists not in curing people but in caring for them." Such thinking is important in the treatment of any patient, and it should never be forgotten in the management of the patient whose disease is related to his

7. Fletcher, C. M., and Gough, J.: Coalminers' Pneumoconiosis, Brit. M. Bull. 7: 42-46, 1950.

8. Parkinson, J.: The Patient and the Physician, Ann. Int. Med. 35: 307-314 (Aug.) 1951.

occupation. All patients seem to feel that the cause of their symptoms can be found in external forces, and they usually attempt such correlations. This state of mind is especially true of the industrial worker, who is usually quite certain of the source of the disease, and professional confirmation merely increases his certainty and reinforces his fears.

Regardless of the pitfalls inherent in making a diagnosis of occupational disease, once the possibility of the existence of such disease is entertained, clinical management of the patient must begin at once. The commonest characteristic of the pulmonary patient is fear. He will not only fear the loss of ability to earn his living but will also be extremely anxious concerning the advent of a chronic, severely disabling disease and death. Although these fears are rarely overt and are even frequently denied, they are nonetheless almost universal in these persons, and immediate measures must be taken to prevent anxiety states. Frequent and firm reassurance by the physician will do much to allay this anxiety and establish a rational attitude of mind. If this reassurance begins when the diagnosis is first made, all further treatment will be more effective and of greater significance to the patient. If reassurance is delayed for a considerable period of time, during which the patient is idle and does no productive work, clinical management becomes increasingly difficult and is frequently ineffectual. All too often, the diagnosis of occupational pulmonary disease is made carelessly in the belief that the patient will thereby benefit from compensation awards and that his employer must continue to pay the worker's wages when he is disabled. Even if this premise were correct, the patient is not best served by being told that his useful life expectancy has been shortened, when such actually may not be the case. An outstanding authority [9] in compensation law has stated the case thus: "No physician may fairly accept the manifest advantages to the medical profession under a good workmen's compensation law without accepting also the responsibilities under that law for newly oriented diagnosis and prognosis."

Thus, when medical considerations are paramount in the mind of the physician, the patient will be provided with the care that will contribute the most to his over-all well-being. These factors consist of attention to the cause of the disease, the capacity of the person to perform work, and the treatment that will be most effective. In addition, if the examination and diagnosis are made without melodrama and without alarm, even the most serious prognosis may be presented to the patient in such a fashion as to make future treatment practical. In the following cases the type of patient in whom the diagnosis of pulmonary disease has produced disability is described.

REPORT OF CASES

CASE 1.—A 39-year-old white miner. (Physician's referral note stated: "There is no question about the diagnosis of silicosis despite the fact that silicosis was not demonstrable on x-ray.")

History.—On admission, the patient complained of cough and continuous chest pain. Both symptoms had begun at about the same time and had become progressively worse. The pain was localized beneath and to the midline of the right scapula and radiated posteriorly and laterally to the right and left. Cough was nonproductive but increased the chest pain. There was no history of hemoptysis. The patient was certain that he had silicosis, because he had been so informed; and the fact that he had a low grade rise in afternoon temperature was submitted by him as proof that he did have silicosis. He had worked as a coal loader for 16 years and at track laying for 3 years. Despite the apparently long occupational history, the patient's work had been intermittent and his actual working time was about one-third of the 19 years. He had not worked for the past four years.

Physical Examination.—The patient was a thin, small white man who was in no apparent distress. His height was 5 ft. 3 in. (160.02 cm.), weight 97½ lb. (44.3 kg.), pulse rate 80, respiration rate 22, temperature 99 F (37.2 C), and blood pressure 120/80 mm. Hg. The teeth were carious. Examination of the chest was negative except for a slight diminution of diaphragm excursion on the right. On motion of the back the patient localized his discomfort beneath the right scapula. The remainder of the physical examination was normal.

Laboratory Findings.—Routine complete blood cell count and urinalysis were normal. Chest roentgenogram was entirely normal, and there was no evidence of cardiac or pulmonary disease. Stool examination showed many adult forms of Enterobius vermicularis. Chest fluoroscopy indicated good ventilatory function with prompt and complete emptying during forced expiration. Maximum breathing capacity was 107 liters per minute. Predicted maximum breathing capacity was 95 liters per minute. While walking up three flights of stairs, the patient's minute ventilation was 14 liters per minute and the oxygen and carbon dioxide of the expired air were 3.93% and 3.39% respectively. (All these figures are well within normal limits.) Electrocardiogram was entirely normal.

On orthopedic consultation, the back pain was reported to be due to chronic strain of the right upper back and scapular muscles and was considered to be postural in cause. The psychiatrist's statement was as follows: "In my opinion he has had a severe anxiety neurosis which has developed into a conversion hysteria, sensory type, with chest pain as the main symptom. The present condition borders on a hypochondriasis, and the length of time in which he has had secondary gain of attention and sympathy (although little welfare compensation) together with a doctor's opinion that he has silicosis (which he has eagerly grasped) make the prognosis not very hopeful."

Comment.—Neither the clinical nor laboratory findings could be considered as being indicative of silicosis. The occupational history indicated that not a great deal of actual working time had been in a seriously dusty exposure. The pulmonary function studies showed adequate pulmonary reserve and no pulmonary dysfunction. After treatment for intestinal parasites had been administered, there were no further rises in afternoon temperature. The patient was given exercises to correct his bad posture, and the back pain diminished greatly. Since he lacked insight, it was felt that psychotherapy would be of little aid, and a regimen of reassurance with palliative medication was instituted. He was told that he did not have silicosis, but it was not suggested to him that he had no disability since it was felt that his belief that he had a disability provided him with a psychological crutch, and it was deemed inadvisable to remove this support from him. Effort was made to encourage him concerning his abilities, and little mention was made of disability. Under this regimen he seemed to improve and became more active while under our care; however, upon returning home, he refused to attempt any type of work.

CASE 2.—A 40-year-old white miner. (Statement from referring physician: "Our x-rays show that he has a chronic lung condition plus bronchial asthma. . . . He is disabled to such an extent that he cannot work.")

9. Donlon, M.: Compensation Aspects of the Pneumoconioses, New York State J. Med. 49: 833-835 (April 1) 1949.

History.—Patient was perfectly well until 1944. Twice during that year he was overcome by smoke during blasting. At that time there developed chest pain, shortness of breath, and headaches that became progressively severer. In 1950 a submucous resection was performed, and his headaches disappeared. Patient stated that he coughed mostly at night and that he wheezed continuously. There was no history of acute asthmatic attacks. He had worked in bituminous coal mines for nine years. This work time was divided as follows: one year, trip rider; one year, driller; one year, helper on cutting machine; two years, floater; and four years, motorman.

Physical Examination.—The patient was a well-developed, well-nourished, slender, alert white man who did not appear to be in acute distress. His height was 5 ft. 7½ in. (171.45 cm.), weight 129 lb. (58.5 kg.), temperature 98.2 F (36.8 C), pulse rate 90, respiration rate 19, and blood pressure 122/75. The chest was symmetrical, but there was marked dorsal kyphosis with lumbar lordosis. There were scattered rhonchi in both lung fields; no wheezes were heard. There was no evidence of respiratory distress while walking. The heart appeared normal.

Laboratory Findings.—The hemoglobin level was 15.5 gm. per 100 cc., red blood cell count 5,590,000, hematocrit 44, white blood cell count 5,850, and differential blood count was polymorphonuclear leukocytes 55.5%, stab forms 0, lymphocytes 37.5%, monocytes 5.0%, eosinophils 2.0%, and basophils 0. Urine had a yellow color, pH 6, and specific gravity 1.025; albumin, sugar, blood, and microscopic tests were negative. Sedimentation rate (corrected) was 5 mm. in 60 minutes. Serologic studies were negative. Three consecutive sputum specimens were negative for acid-fast organisms. A heterogenous normal bacterial flora was seen in the sputum. Chest roentgenogram revealed a moderate exaggeration of the bronchovascular markings, but no nodulation was seen. There was no evidence of pleural, parenchymal, or cardiac disease. Chest fluoroscopy showed that during forced respiration, diaphragm motion was equal bilaterally to the extent of about three interspaces. Ventilation appeared to be equal and complete bilaterally except for both apexes. In the lateral view, the costosternal angle did not clear completely during forced expiration, and this was interpreted as having been produced by upper lobe emphysema. There was marked kyphosis in the thoracic region with a slight left scoliosis. Motion of the spine was free.

Comment.—The only positive findings of any consequence in this patient were those of kyphosis and upper lobe emphysema, which was probably secondary to the structural deformity of the spine. A diagnosis of pneumoconiosis was not justified by the laboratory findings, the physical examination, or the occupational history. The diagnosis of bronchial asthma could not be verified by either the history or the physical findings. Discussions with the patient brought out the fact that his illness had become a matter of compensation litigation. His greatest concern was that return to work would be prejudicial to his claim. There was no question of malingering, but the patient had been convinced by his physician that he must not work. He was placed on intermittent positive pressure breathing with a bronchodilator by aerosol, and 300,000 units of penicillin were administered daily for one month. Constant reassurance was provided, and he improved rapidly so that by the time of discharge he was able to walk one to two miles without distress. Six months after discharge, the patient was still working without difficulty.

CASE 3.—A 44-year-old white miner. (Referral note: "Granular stage of silicosis. . . . He may be slightly dyspneic on exertion through the effects of the silicosis and later may develop some complication of lung or vascular system.")

History.—Approximately five years prior to admission, the patient began suffering from a sharp substernal pain. The pain would persist for about one-half hour and occurred once or twice daily. The attacks became progressively severer and more frequent, and the patient stopped work after about one year. On several occasions he was taken to the hospital and given morphine for pain. After he had stopped working, the pain became less frequent and occurred about once or twice weekly, always between the hours of 11 p. m. and 1 a. m. He stated that one physician had told him, "If I had what you have, I would never go back to work again." He had gained about 20 lb. (9.1 kg.) in weight since he had stopped working. He had worked in the bituminous coal mines for 20 years, as follows: 3 years at the tipple loading railroad cars, 8 years as a loader in the mine, and 9 years laying track. The descriptions of these jobs did not indicate excessive dust exposure.

Physical Examination.—The patient was well developed and well nourished and in no apparent distress. His height was 5 ft. 3¾ in. (161.83 cm.), weight 164 lb. (74.4 kg.), pulse rate 72, respiration rate 18, and blood pressure 130/80 mm. Hg. There were no abnormal physical findings referable to the pulmonary or cardiovascular systems.

Laboratory Findings.—Routine complete blood cell count and urinalysis were normal. Blood chemistry tests were negative. While the chest roentgenogram showed the bronchovascular markings were slightly exaggerated, they were not unusual for this patient's age. There was no hilar enlargement and no nodulation. In the fluoroscopic examination there was no evidence of impairment of ventilatory function. Maximum breathing capacity was 129 liters per minute. Predicted maximum breathing capacity was 128 liters per minute. The resting electrocardiogram was within normal limits.

The psychiatrist's statement was as follows: "My impression is of a cardiac neurosis, with features of both anxiety neurosis and conversion hysteria, in an hysterical personality who has driven himself to activities and achievements which constituted strain for himself, and who has been able to allow himself a curtailment of activities only on the grounds of the heart condition he believes he has."

Comment.—Since the history of exposure to dust was minimal, in the absence of any of the necessary criteria for a diagnosis of silicosis and in view of the adequate pulmonary reserve, this patient was treated only from the point of view of the psychiatric findings. He was given 50 mg. of methantheline (banthine®) bromide three times a day for four days and then 50 mg. every two days. Constant reassurance was provided concerning the absence of organic disease, and the patient was advised that he could and should continue to work. Under this simple regimen his outlook improved rapidly and his symptoms decreased markedly both in severity and frequency. Six months after discharge he was working every day without difficulty.

SUMMARY

Management of the patient begins when the disease is first suspected. The diagnosis must be based on adequate clinical and laboratory findings and a history of sufficient exposure to deleterious dust. An objective appraisal of all the circumstances that have produced the disability will result in the greatest benefit to the patient, particularly if the prognosis is not made to appear gloomy. Parenteral antibiotic therapy, aerosol bronchodilators, and intermittent positive pressure breathing have been proved effective and have resulted in rapid improvement, both subjectively and objectively. Close attention to nutritional requirements and foci of infection contributes to the well-being of the patient. General rehabilitation measures and return to work result in continued physical and mental improvement. The patient with chronic pulmonary disease must be regarded as a person subjected to environmental factors that influence his ability to improve. The disease itself is a functional phenomenon to which he can and must be taught to adjust.

SOME PROBLEMS IN ROENTGEN DIAGNOSIS OF SILICOSIS

Eugene P. Pendergrass, M.D., Philadelphia

The roentgenologic aspects of silicosis are well known to many physicians interested in occupational diseases of the chest. The criteria for the roentgen diagnosis of silicosis have been described and effectively correlated with experimental and pathological observations. In spite of all the information available to those who are called upon to give opinions on workers in a silica hazard, oftentimes it is impossible to render a correct interpretation and on other occasions the wrong diagnosis is made. My personal experience with some of these difficulties has prompted the selection of three totally different observations or groups for consideration.

ANALYSIS OF OBSERVATIONS

It is generally conceded that the roentgen examination, properly done, is the most precise method available for demonstrating visible shadows of pathological changes produced by silicosis. In this country the diagnosis of silicosis is not made, as a rule, in the absence of positive roentgen evidence of the condition. One may even feel that if there is no roentgen evidence of silicosis, then any unseen effects of silica in the lungs are not significant. There is a general impression among radiologists and clinicians that lesions 2 to 3 mm. in diameter are recorded on the conventional roentgenogram in most instances. I myself have been reconciled for years to the fact that small subpleural nodules may not be distinctly recorded on the roentgenograms so that they can be recognized and interpreted. More recently, the observations of Birkelo and associates [1] and of Garland [2] have shown that the personal errors in film interpretation are real. For the most part, however, the failure to record larger lesions in conventional roentgenograms is not generally appreciated. It is such cases that I would like to direct attention to.

Group 1.—About 1944 I began to make roentgen examinations of the chests of patients who had died, in order to compare them with the premortem examinations. I was surprised to find that I was missing certain lesions that should have been seen at prior examinations and also others that were not observed even when the roentgenograms were later restudied. The following examples will serve to illustrate the type of information one might obtain by utilizing the postmortem method of roentgenography.

CASE 1.—This man had been treated for polycythemia since 1938. He died on Feb. 7, 1948, with a blood picture that looked very much like acute leukemia. The roentgenograms of this particular patient show how readily one can overlook a 1 cm. lesion in the lung, the shadow of which is superimposed on a rib.

CASE 2.—This patient, a 27-year-old Negro woman, in her first hospital visit had a mass in the upper quadrant of the right breast. The overlying skin was warm and slightly edematous. The mass, 7 by 12 cm. in size, was attached to the overlying skin but not to the chest wall. The patient was intensely jaundiced. A roentgen examination on Feb. 5, 1949, showed practically nothing of any significance. The patient died, and at autopsy another examination of the chest was done, 20 days after the previous one. The roentgen examination of the excised lungs showed numerous lesions (2 to 3 cm.) throughout both lungs. In my opinion these lesions were present in the earlier examination but for some reason were not demonstrable on the conventional roentgenogram.

CASE 3.—A 43-year-old man with a large lesion in the region of the left hilum died three days after a head operation. The postmortem roentgenogram of the excised lungs showed a metastatic lesion 5 to 7 cm. in diameter that had not been seen in premortem examinations made three days before.

All of these patients had round lesions, some of which were in the midlung fields. They serve to illustrate that lesions (1 to 5 cm.) may be present on the conventional roentgenograms and either not be seen or not be recorded on the roentgenogram in sufficient contrast to be identified by the radiologist. From experience it is known that body-section roentgenography does demonstrate some of these lesions better than conventional roentgenography. For the present, therefore, it would seem advisable to employ body-section roentgenography in questionable cases. More important, I believe the whole problem of chest roentgenography needs reevaluation. In addition, efforts must be made to improve present techniques of roentgenography.

Group 2.—The second group of cases is concerned with the roentgen diagnosis of carcinoma in persons who have silicosis. We are now living in a period in which there is a high index of suspicion of lung cancer. Although the incidence of carcinoma of the lung occurring in silicotic persons is not high, such lesions do occur. Isolated conglomerate or small massive silicotic lesions in the lungs without nodulation present a difficult problem of diagnosis. Two patients so afflicted came under my observation, and in both instances an incorrect diagnosis of carcinoma was made. The isolated silicotic lesion was demonstrated at subsequent operation, and, in addition, many silicotic nodules could be seen in the microscopic slides. These had not been seen in the roentgenograms.

Group 3.—This last group of cases is of interest because the long-time follow-up examinations present findings that may be of prognostic and diagnostic assistance regarding silicotic persons. Some of the silicotic lesions around the hila look like mediastinal tumors. I have observed a migration of massive lesions from the upper peripheral zones of the lung toward the hilum in certain instances. The migration of these lesions may take 10 or more years to travel from the periphery of the lung to the hilum. This has been a very interesting observation and has been helpful in explaining some of the prominent shadows seen adjacent to the hilum or hila in certain patients. Before observing such changes in the follow-up examinations, I had had difficulty in explaining

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1. Birkelo, C. C., and others: Tuberculosis Case Finding: A Comparison of the Effectiveness of Various Roentgenographic and Photofluorographic Methods, J. A. M. A. **133**: 359-366 (Feb. 8) 1947.

2. Garland, L. H.: On the Reliability of Roentgen Survey Procedures, Am. J. Roentgenol. **64**: 32-41 (July) 1950.

the pathological physiology of the silicotic lesions found in the mediastinal region. One of my former explanations was that a lesion in the apical portion of the lower lobe produced a shadow that was superimposed on the hilum. This may occur, but migration of lesions also takes place.

SUMMARY

Postmortem and postoperative studies reveal certain lesions in the lungs that are not recorded on conventional roentgenograms. Some of these lesions are more than 1 cm. in diameter. Isolated conglomerate or small massive silicotic lesions are sometimes called carcinoma of the lung, especially in those instances in which one does not see roentgen evidence of nodulation. Migration of massive silicotic lesions of the upper lobes toward the hilum has been demonstrated in certain patients who were followed up for 10 or more years. The roentgen appearance of a silicotic lesion that has migrated toward the hilum oftentimes is that of a mediastinal tumor.

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RECENT ADDITIONS TO KNOWLEDGE OF POLIOMYELITIS

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During the past two years, several hundred articles dealing with many phases of the study of infantile paralysis have appeared in the medical press. While not all of the significant contributions that have been published during this period are considered, aspects to be covered are etiology, pathogenesis, factors precipitating paralysis in experimental animals and man, immunization studies, and finally, the very important discovery that the virus can be grown in cultures of non-nervous tissue.

ETIOLOGY

Cross immunity tests have shown that the poliomyelitis viruses can be separated into three broad antigenic groups. This investigation, involving several hundred strains of the virus, has been completed, and a report of the results of the first 100 strains typed has already been published. The program, guided by the special Committee on Typing of the National Foundation for Infantile Paralysis, was carried out by four teams of investigators located at the universities of Pittsburgh, Kansas, Utah, and Southern California. These studies were begun in 1948 and completed three years later.[1]

Among the first 100 strains typed, 85 were Brunhilde-like or type 1; 12 belonged to the Lansing group or type 2; and only three resembled the prototype strain of Leon virus, namely, type 3. The majority of the original strains were isolated in monkeys. More recently, by the use of tissue cultures, a number of new strains of type 3, or the Leon type of virus, have been obtained, suggesting the possibility that tissue cultures are a better medium for isolating type 3 strains. It has also been found that more than one type of poliomyelitis virus may be present in a single epidemic in a community. For instance, Bodian [2] has reported the isolation of strains of types 1 and 3 from young children using the same playground.

Bodian has also produced evidence to indicate that second attacks of paralytic poliomyelitis in human beings are due to reinfection with virus of an antigenic type different from that producing the first attack. He gave details concerning a boy who experienced his first attack at the age of 3 years and his second attack at the age of 12. At the time of his second attack, this child had a high level of antibodies against Brunhilde virus, while a strain of Leon-like virus was isolated from concentrated suspensions of his stools. Five years later this boy's serum also contained antibodies against Leon virus in high titer. Bodian concluded, therefore, that the first paralytic attack in this child was probably caused by a virus of the Brunhilde type and the second attack by a strain belonging to the Leon group.

Pathogenesis, virulence, invasiveness, and antigenicity may vary among different strains in one type. For instance, Melnick reports that the Y-SK strain, which belongs to the Lansing group, will stimulate the formation of antibodies when fed to cynomolgus monkeys. The original Lansing strain, however, appears to have lost that capacity, perhaps as a result of repeated passage in laboratory animals.

A number of investigators have recently shown that both Coxsackie virus and the virus of poliomyelitis can occur in the same epidemic and indeed in the same patient. In one such individual, poliomyelitis virus was found in the feces for a somewhat longer period of time than Coxsackie virus. A detailed study of an epidemic at Easton, Pa., carried out by Melnick and his collaborators,[3] revealed the fact that half of the poliomyelitis patients examined, particularly those with the paralytic form of the disease, were excreting both viruses. It is not yet possible to decide, in such a situation, to what extent each virus was responsible in the over-all pattern of the disease. Both viruses have also been found in nature in flies and in sewage.

PATHOGENESIS

During the past year, a significant advance has been made by the discovery of viremia in two species of primates. Paul had suggested previously that it was entirely possible that there might be a short phase of viremia during the incubation period of poliomyelitis in humans. In support of that prediction, he had quoted some unpublished experiments of Horstmann, in which she had found viremia in cynomolgus monkeys infected by oral administration of the virus. So far, viremia in humans has been

Read before the Section on Nervous and Mental Diseases at the 101st Annual Session of the American Medical Association, June 12, 1952.

1. Committee on Typing of the National Foundation for Infantile Paralysis: Immunologic Classification of Poliomyelitis Viruses: A Cooperative Program for the Typing of 100 Strains, Am. J. Hyg. **54**: 191-204, 1951.

2. Bodian, D.: Second Attacks of Paralytic Poliomyelitis in Human Beings in Relation to Immunity, Virus Types and Virulence, with Report of 2 Cases, and 4 Other Individuals in Baltimore, 1944, Infected with Virus of Leon Type, Am. J. Hyg. **54**: 174-190, 1951.

3. Melnick, J. L., and others: An Epidemic of Paralytic Poliomyelitis Characterized by Dual Infections with Poliomyelitis and Coxsackie Viruses, J. Exper. Med. **94**: 471-492, 1951.

demonstrated on two occasions only. Both of those persons were bled early in the course of abortive or nonparalytic attacks. The case reported by Ward, Horstmann, and Melnick occurred in a 9-year-old girl, while the patient studied by Koprowski, Norton, and McDermott was a man 29 years of age.

More recently, Horstmann announced [4] that, following oral infection with poliomyelitis virus, 7 of 10 cynomolgus monkeys and 3 of 4 chimpanzees showed viremia early in the incubation period. Viruses of both the Brunhilde and the Lansing types were demonstrated in the blood stream of these primates, usually between the fourth and the sixth day after they had ingested one or the other of those viruses. The interval of time between viremia and the subsequent appearance of paralysis varied between three and seven days in those monkeys. Bodian [5] reported similar findings, and in addition he suggested that virus multiplication in the body may occur in succession in at least three different phases, which he has referred to as the alimentary, vascular, and neural phases.

In this connection, it is interesting to note that Wenner and Rabe have reported the recovery of virus from the regional lymph nodes of six out of nine fatal human cases of poliomyelitis. They made the assumption that, during the invasive period, virus spreads from a position in the gastrointestinal tract into lymph channels that empty into the blood stream.

Sabin has stated, "Excepting artificial conditions, entry of poliomyelitis virus by way of the mouth can justifiably be regarded as the usual mode of infection." He is convinced that "human feces derived from patients and healthy carriers is the most significant source of virus in nature." It is now generally agreed that virus is transmitted more readily in the intimacy of household association than under any other conditions.

FACTORS PRECIPITATING PARALYSIS

The relationship of physical activity at the time of onset of poliomyelitis to the severity of the disease was studied by Horstmann. She found that such activity during the first brief phase had no effect. During the second or more acute febrile stage of the illness, unusual physical exercise was clearly associated with a significant increase in the incidence and severity of subsequent paralysis.

The increased risk of poliomyelitis following tonsillectomy has been studied by Anderson and associates in man,[6] and by Faber and his colleagues in monkeys. The former reported that the risk of developing severe poliomyelitis was at least three times as great among persons who had undergone tonsillectomy within one month prior to exposure to the virus as among a comparable group not subjected to that operation. The danger of bulbar infection developing, however, was 11 times as great. Faber studied cynomolgus monkeys that had been prepared by severing their olfactory tracts to prevent the migration of virus to the brain along those nerves. If poliomyelitis virus was applied to the pharynx of such monkeys following enucleation of the tonsils, bulbar paralysis resulted. This could be prevented by painting the inoculated area of the pharynx with 2% tincture of iodine.

Anderson and his colleagues have carried out a careful review of 75 cases of poliomyelitis in pregnant women, which were recorded during the great Minnesota outbreak of 1946. They found that the attack rate in nonpregnant females was 47 per 100,000, as compared to 74 per 100,000 in a group of pregnant women of similar age. No evidence was uncovered, however, of a greater severity of the infection among the latter.

Shwartzman [7] has published the very interesting observation that corticotropin (ACTH) and cortisone in combination, or cortisone alone will produce a marked enhancement of poliomyelitis in mice and will increase the susceptibility of hamsters to the paralytic disease. The enhancement manifests itself in increased severity of symptoms, shortening of the incubation period, marked reduction in survival time, and a high mortality rate. It appears that there is a relationship between adrenocortical function and susceptibility of those animals to infection. Studies now in progress would suggest that, under certain conditions, experimental poliomyelitis in monkeys also may be accelerated by pretreatment of the animals with cortisone.

The possible relationship between various types of inoculations and poliomyelitis was discussed at a recent meeting convened by the United States Public Health Service. That group felt that there is no definite evidence of any increase in the number of cases of poliomyelitis as a result of injections. There is, however, evidence that injections for the prevention of diphtheria, whooping cough, and possibly tetanus when given during an epidemic of poliomyelitis may, on rare occasions, localize the paralysis in the inoculated arm or leg.

IMMUNIZATION STUDIES

If cynomolgus monkeys are fed poliomyelitis virus, serum antibodies appear early, whether or not paralysis develops. When paralysis does occur as a result of oral administration of virus, antibodies are usually present on the first day of paralysis.

Koprowski, Jervis, and Norton [8] have recently carried out a study of the development of Lansing type antibodies in man. Twenty human volunteers, of whom 15 did not have any demonstrable neutralizing antibodies, were fed a strain of living poliomyelitis virus adapted to cotton rats. Virus was subsequently found in the stools of 12, or 80%, while all 15 of those individuals became immune to the MEF_1 strain of type 2 poliomyelitis virus. Fortunately no signs of illness were noted in any of them.

The presence of circulating neutralizing antibodies however, did not preclude the temporary establishment of a fecal carrier state. The latter situation was demonstrated in 4 persons out of 15, or 26.7%, of those who

4. Horstmann, D. M.: Poliomyelitis Virus in Blood of Orally Infected Monkeys and Chimpanzees, Proc. Soc. Exper. Biol. & Med. **79**: 417-419, 1952.

5. Bodian, D.: A Reconsideration of the Pathogenesis of Poliomyelitis, Am. J. Hyg. **55**: 414-438, 1952.

6. Anderson, G. W.; Anderson, G.; Skaar, A. E., and Sandler, F.: The Risk of Poliomyelitis After Tonsillectomy, Ann. Otol., Rhin. & Laryng. **59**: 602-613, 1950.

7. Shwartzman, G.: Enhancing Effect of Cortisone upon Poliomyelitis Infection (Strain MEF_1) in Hamsters and Mice, Proc. Soc. Exper. Biol. & Med. **75**: 835-838, 1950.

8. Koprowski, H.; Jervis, G. A., and Norton, T. W.: Immune Responses in Human Volunteers upon Oral Administration of a Rodent-Adapted Strain of Poliomyelitis Virus, Am. J. Hyg. **55**: 108-126, 1952.

were either originally immune or else had developed antibodies as a result of having ingested virus.

Hammon [9] has pointed out that, since a vaccine is not available at the present time, the possibilities of passive immunization merit careful consideration. Bodian demonstrated in monkeys [10] that low levels of serum antibody, produced by passive immunization before fixation of the virus in nervous tissues, are capable of preventing paralysis due to peripherally introduced virus. This prophylactic effect was obtained with human gamma globulin, which contains antibodies against all three types of virus. A field trial of the potentialities of this procedure in man is now under way.

TISSUE CULTURE

Although the initial reports of the cultivation of poliomyelitis virus in cultures of non-nervous tissue were published in 1949, by Enders, Weller, and Robbins, much additional progress in this field has occurred during the past two years. Enders and his associates have been able to show that all three types of poliomyelitis virus will multiply on cells grown from fragments of monkey or human tissue when the latter are placed in small Erlenmeyer flasks or test tubes and bathed with a suitable nutrient medium. They used human embryonic skin, muscle or brain, human kidney, prepuce, or uterus. Other investigators have worked with human or monkey testis and with monkey kidney.

One of the most useful types of tissue culture is a roller tube culture. This is nothing more than a test tube, on the inside of which minute fragments of human or monkey tissue have been distributed in a sticky film of plasma. Afterwards, a mixture of salt solution, horse serum, beef or chick embryo extract, or a suitable synthetic medium is added. The test tube is then placed in a drum inside an incubator. As the drum slowly revolves, it causes the serum to wash over the pieces of living tissue. Soon, new cells are produced and spread over the inner surface of the test tube. Their growth may be readily followed in a microscope.

After these new cells are growing well, if a small amount of poliomyelitis virus is added, cytopathogenic effects soon become apparent. The lethal action of poliomyelitis virus on those growing cells is easily seen in a microscope. Furthermore, if serum containing antibodies to the same type of virus as that used to infect the cells is introduced, the otherwise susceptible cells will not die. If, on the other hand, the added serum contains antibodies to a different type of virus than that used to infect the cells in the first place, those cells will succumb just as if no serum at all had been introduced.

It has thus been possible for Robbins, Enders, Weller, and Florentino [11] to describe a method for the direct isolation and serological identification of virus strains from patients by the tissue culture technique. Previously it had only been feasible to carry out those procedures by the use of monkeys.

Strains of Brunhilde and Lansing viruses adapted to growth in tissue culture have been employed by Svedmyr, Enders, and Holloway [12] as antigens in complement fixation tests for the diagnosis of poliomyelitis. Specific antibodies were demonstrated in the serums of patients with infantile paralysis as well as in hyperimmunized monkeys. Serums obtained from patients a year or more after the termination of their respective illnesses, when tested at the same time as earlier specimens, have shown a marked drop in the titer of these complement-fixing antibodies. Other investigations have suggested that the titer of complement-fixing antibodies may show a significant decrease as early as three months after the onset of the infection.

Furthermore, Enders and co-workers have reported that the pathogenicity for monkeys of a Brunhilde-like strain of poliomyelitis virus may be reduced by repeated cultivation in vitro. Whether a long-continued series of such tissue cultures will eventually lead to the development of a nonpathogenic strain that retains its original antigenicity has not yet been determined.

SUMMARY

During the past two years a number of significant advances have been made in the field of poliomyelitis but only a few are mentioned in this discussion. A report was published dealing with the first 100 strains of virus that have been classified into their broad antigenic groups. Three different immunogenic types were found. It was shown that second attacks of poliomyelitis may be caused by successive infections with different immunogenic types of the virus. Viremia has been demonstrated during the incubation period of the experimental disease in cynomolgus monkeys and chimpanzees. It has been proved that in monkeys prophylactic injections of a blood fraction containing antibodies will prevent paralysis. The effects of such inoculations in human beings are now under investigation. Techniques have been developed for in vitro growth of virus in tissue cultures. The potentialities of this procedure for advancing the study of poliomyelitis are very great.

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Indiscriminate Therapy.—The availability of potent drugs manifesting remarkable curative effects in serious conditions is no excuse for their promiscuous use in conditions in which simpler, safer and cheaper measures may be equally effective. The wide use of penicillin and other antibiotics, for example, for many minor disorders is to be deprecated, particularly in such conditions as the common cold in which they are ineffective. The gastrointestinal disturbances or allergic reactions accompanying the use of some of these agents may induce a greater disability than the primary disease which, as in the case of the common cold for example, may be entirely unresponsive to these drugs. The wide use of cortisone and corticotropin as panaceas is similarly to be deprecated. The wise physician will not be stampeded into the use of a drug by the enthusiasm which heralds the new, but will be guided by sound principles of scientific medicine.—A. Grollman, M.D., Ph.D., The Use and Abuse of Drug Therapy, *The Journal of the Omaha Mid-West Clinical Society*, August, 1952.

BENIGN AND MALIGNANT DERMAL NEOPLASMS

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Uniformity or general agreement concerning the classification of dermal neoplasms does not exist, especially because more than one type of mesenchymal or mesodermal tissue often participates in the neoplasms, regardless of whether such neoplasms originate in connective tissue, muscle, nerve, or vascular tissue. Differences in emphasis among different pathologists explain a great part of the present confusion regarding classification. Furthermore, it is difficult at times to differentiate between benign and malignant neoplasms. In addition, some conditions that are grouped as benign dermal neoplasms, such as cicatrix and various forms of nodular subepidermal fibrosis, scarcely can be regarded as new growths or tumors in the ordinary sense; yet generally they are classified as such. The same is true of most forms of cutaneous xanthomatoses, which are caused by a disturbance in the metabolism of lipids and are not true tumors.

The scope of this presentation does not permit discussion of all dermal neoplasms or of such tumors as the osteogenic tumors and the large, deep-seated fibromas and sarcomas that primarily are in the realm of the surgeon. The lymphoblastomas also will not be considered. Several general reviews and textbook discussions of dermal neoplasms are available.[1] The bibliography has been limited to recent comprehensive articles or reviews.

Small dermal and subcutaneous tumors, however, should be discussed. The classification used in this paper is offered merely as a working basis and does not conform always to the diagnoses listed in the "Standard Nomenclature of Diseases and Operations."[2] Following is a classification of benign dermal neoplasms:

Cicatrix, keloid
Nodular subepidermal fibrosis
  Dermatofibroma, histiocytoma, sclerosing hemangioma
Knuckle pads, cutaneous tags
Solitary fibroma, myxofibroma, desmoid
Reticulohistiocytoma
Neurofibroma, neuroma, ganglioneuroma, glomus tumor
Blue nevus, Mongolian spot
Myoma, leiomyoma, granular cell myoblastoma
Hemangioma, lymphangioma
Granuloma pyogenicum, hemangiopericytoma
Lipoma, chondroma, osteoma, synovioma

BENIGN DERMAL NEOPLASMS

Cicatrix.—Scars that result from various dermatoses and burns as a rule are not diagnostic as to type or cause either clinically or histologically, nor do they, except infrequently, give rise to malignant change. The scars that are associated with radiodermatitis and radiokeratosis are diagnostic clinically and histopathologically. The significant findings in these lesions are the epidermal changes, atrophy of the dermal appendages, and obliterative changes in the vessels, together with homogenization of the connective tissue. Squamous cell carcinoma, which often may simulate fibrosarcoma, occurs in as many as 20% of cases of radiodermatitis, but true sarcomas following this condition have been reported.[3]

Keloid.[4]—Hypertrophic scarring merges with formation of keloids. Sharp clinical or histological distinction between the two is not possible. Histologically, keloids are composed of swollen bundles of collagenous fibers. The superficial bundles take a course parallel to the epidermis, whereas the others interlace in all directions with great irregularity. Keloids display varying degrees of vascularity, which is more prominent in the earlier stages of the lesions. The keloid is not encapsulated but shows simply an increase in collagenous tissue and, therefore, scarcely can be considered to be a true tumor. It rarely undergoes malignant change. Judicious radiotherapy is the method of choice.

Nodular Subepidermal Fibrosis.—This is a common lesion that usually is encountered as one or more nodules ranging from 0.5 to 3 cm. in diameter. These nodules ordinarily form a domed, smooth elevation, although sometimes the lesion is depressed and is surrounded by a shallow moat-like furrow. The nodule is freely movable but may be firmly attached to the overlying epidermis. The nodule may have a light yellow hue, simulating that of a xanthoma, or it may be brown or at times blue-brown so that it may be mistaken for a malignant melanoma. The lesions occur predominantly on the extremities and in adults.

On the basis of studies made by Rentiers and me [5] of 95 patients, together with subsequent observations of more than 200 cases encountered in adults, I believe that nodular subepidermal fibrosis [6] is the correct designation and that this condition is not a true tumor. Histologically, it can be divided into dermatofibroma, histiocytoma,[7] and sclerosing hemangioma.[8] It is difficult to reconcile differences in the findings of Rentiers and me, on the one hand, and the findings of Senear and Caro [7b] and of Gross and Wolbach.[8] The latter two authors included lesions of the face in children who had a history of an antecedent hemangioma. This accounts for their term "sclerosing hemangioma." Since the article of Gross and Wolbach appeared, I have failed to obtain a history of an antecedent hemangioma in a total of more than 200 patients seen at the Mayo Clinic in whom biopsies were done. A history of preceding trauma occurs frequently. The lesions in only about a third of the cases were associated with deposition of hemosiderin or lipids, and in considerably less than a dozen cases sufficient vascularization was revealed to warrant a designation of sclerosing hemangioma. It is my impression that the various divisions of nodular subepidermal fibrosis are all part of the same process. A few reports in the literature indicate that malignant change occurs in this group, but I have yet to encounter it. Treatment involves excision or cautery simply for cosmetic reasons.

From the Section of Dermatology and Syphilology, Mayo Clinic.

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The bibliographic references have been omitted from THE JOURNAL because of lack of space; they are, however, included in the author's reprints.

Cutaneous Tags.[9]—These may be referred to as acrochordon or papilloma. They are benign, pinhead-sized to pea-sized, soft, papular, pedunculated lesions that occur often as filiform tags and are treated only for cosmetic reasons. Fulguration of the base usually is sufficient to destroy the lesion.

Knuckle Pads.[10]—Lesions of this type occur as fibrous thickenings that vary from the size of a pea to that of a hazelnut. These pads occur usually on the extensor surfaces of the proximal interphalangeal joints of the fingers and occasionally on the toes. They may be associated with Dupuytren's contracture. The pathological changes are similar to those seen in the dermatofibromatous type of nodular subepidermal fibrosis. A history of preceding trauma may be obtained. Because of their location, knuckle pads must be distinguished from Heberden's nodes, gouty nodules, benign lesions of the synovial lining, and even glomus tumors.

Uncommon Fibromatoses.—Stout [11] referred to a form of palmar and plantar fibromatosis that often is associated with Dupuytren's contracture and that recurs locally if it is not excised completely. Penile fibromatosis (Peyronie's disease) consists of fibrous proliferation, stiffening, and deformity of the penis. Nodules like those seen in Dupuytren's contracture also may be formed. These conditions are not true neoplasms, nor are fibromatosis colli (congenital wry neck or torticollis), diffuse progressive myositis fibrosa, or hereditary polyfibromatosis.

Fibroma, Myxofibroma, and Desmoid.—True solitary fibroma of the skin is uncommon and presents no distinctive clinical features. Myxofibromas and myxomas of the skin are pathological curiosities that may be diagnosed only on the basis of the histological findings of mucin mixed with fibrous proliferation. Desmoids [12] are rare cutaneous tumors with a definite pathological pattern.

Reticulohistiocytoma Cutis.—This is a relatively new condition that has been confused in the past with both ganglioneuroma and granular cell myoblastoma. The lesions consist of multiple small papules that are distributed chiefly over the extensor surfaces of the extremities but also occur on the face. Many of the papules or nodules have a xanthomatous hue, and systemic conditions, such as arthralgias or disease of the thyroid, may be associated. Occasionally, only a solitary nodule may be present, and in such cases no systemic disorder occurs.[13]

Diagnosis is established histologically on the basis of the presence of large, bizarre, multinucleated, giant cells with large, pale nuclei and dark nucleoli. The giant cells are separated by fibrous connective tissue. Special stains fail to reveal the presence of lipids. Granules cannot be demonstrated in the cytoplasm of the giant cells, which are essentially histiocytes, and the Nissl granules present in ganglioneuroma cannot be shown by means of the thionine stain. Caro and Senear [14] demonstrated the histiocytic nature of these giant cells by means of vital staining with colloidal iron. Histochemical studies with microincineration revealed no silicon, but a great increase of iron in the giant cells was noted. No treatment exists at present for this disease.

Neurofibroma (Recklinghausen's Disease)[15].—This disease, with all its ramifications, is familiar to dermatologists, as are those rare instances of true neuroma or ganglioneuroma of the skin.[16] The pathological picture of the cutaneous tumor in neurofibroma is distinctive and consists of sharply circumscribed bands of pale, fine, spindle-shaped fibrils that often present a whorl-like arrangement and resemble the cells seen in neural tissue. The cells and collagen fibers in neurofibromas are much more delicate than those in nodular subepidermal fibrosis. Nonmedullated neural fibrils can be demonstrated by use of the Bodian method of staining. Treatment is surgical for cosmetic purposes or when pressure on a nerve results in pain. Sarcomatous change occurs apparently in some of the deeper and larger tumors.

Glomus Tumor (Glomangioma).[17]—Glomus tumor occurs usually as a solitary, bluish, painful nodule that in itself is distinctive. As many as 90 nodules, however, may be present, and, because at times they may be nonpainful, confusion with malignant melanoma may occur. Surgical excision is indicated for the painful lesions.

Blue Nevus.[18]—This lesion is a sharply circumscribed, round or oval, flatly elevated papule or nodule that varies from 2 to 15 mm. in diameter. The lesions usually are single, although multiple tumors can occur. Occasionally, large plaques have been encountered.[19] The color varies from blue or mottled blue to blue-black, blue-gray, steel-blue, or black. Clinically, diagnosis can be made when the physician encounters a lesion of such color that was present at birth or that developed shortly after birth and that has undergone no subsequent increase in size. When the lesion is steel-blue or black or when it develops later in life, pathological studies may be necessary to distinguish it from a malignant melanoma.

In 1939, Kahler and I reported 65 cases of blue nevi, in 38 of which pathological studies were done.[18] I now have made histological studies on 180 blue nevi, which indicate that the condition is not so uncommon as was formerly thought. In the original series, four cases occurred in which a lentigo or junction nevus, or both, revealed ordinary nevus cells lying within or just beneath the epidermis and in which the blue nevus cells occurred deeper in the cutis. No connection between the two types of nevus cell was demonstrable. I have not seen this phenomenon subsequently, and I am firmly convinced that the blue nevus is independent of an ordinary nevus. However, if both types of nevus cells originate from the neural crest, then it could be expected that the dendritic cell seen in blue nevus represents a cell that has failed to migrate as far as the epidermis and that, because of its situation in the cutis, it may be larger than the dendritic cells in the epidermis. It should be recognized, however, that the dendritic cell (melanocyte) is the only pigment-forming cell in the epidermis.[20]

The histological picture of the blue nevus is characteristic and consists of long, bipolar, dendritic cells laden with melanin. These cells may not be recognized at times unless staining with silver nitrate is employed to bring out the melanin. Thus, older lesions in which some fibrosis has taken place may erroneously be diagnosed as fibroma or nodular subepidermal fibrosis. Jadassohn found that

the cells of blue nevus gave a positive reaction with dopa. Fitzpatrick [21] has been unable to obtain a good tyrosinase reaction in several blue nevi that he has studied, but this also is true of the ordinary pigmented nevus and probably means that the lesions were old and, therefore, inactive in regard to further formation of tyrosine. The dendritic cell of the blue nevus is many times larger than the dendritic cell of the epidermis (melanocyte).[22] Histologically, a form of blue nevus also is seen that Allen [23] referred to as a cellular blue nevus. A rapid glance at sections stained with hematoxylin and eosin apparently discloses nevus cells in intimate relation to the dendritic cells of the blue nevus. Again, however, if the section is stained with silver nitrate, the round to oval cells that appear to be ordinary nevus cells can be shown to possess bipolar dendritic processes that are not found in ordinary nevus cells. I cannot agree with Stout [1c] and others that blue nevi are variants of ordinary pigmented nevi.

The so-called cellular type of blue nevus just mentioned frequently has been mistaken for malignant melanoma. The blue nevus fundamentally is a benign lesion and, like ordinary pigmented moles, rarely undergoes malignant change except when subjected to long and repeated trauma and irritation. In none of the series of blue nevi that I have studied has there been any evidence of malignant change, with the exception of one case in which a blue nevus in the foot displayed metastasis to the groin. The patient in this case had several other blue nevi but apparently had no ordinary pigmented nevi. The patient was still alive and well three years after metastasis to the groin occurred. This patient was a Mexican, and the material in this case was supplied by Dr. Couperus. I am aware of one or two other cases in which a blue nevus underwent malignant change with or without metastasis and several cases of melanosarcoma arising from blue nevi have been reported.[24] A blue nevus that has been present since birth does not require excision except for cosmetic reasons. Those lesions that develop later in life may be confused with malignant melanoma and may require wide excision.

Mongolian Spot.—Blue nevus can be distinguished histologically from a Mongolian spot by the wider separation of the cells in a Mongolian spot, although the dermal dendritic cells are similar in size and shape. In some cases, Mongolian spots have persisted throughout life.[25]

Myoma.[26]—Lesions of this type can be divided into simple solitary dartoic myoma, leiomyoma, and granular cell myoblastoma. Leiomyomas may vary in number from single lesions to hundreds of tumors.[27] Like glomus tumors, they usually are painful and sensitive to pressure, but nonpainful forms may occur. They are described adequately in textbooks on dermatology.

Granular Cell Myoblastoma.[28]—This lesion presents no distinctive clinical picture, although, when it involves the mucous membranes, pseudoepitheliomatous hyperplasia may occur. The histogenesis of granular cell myoblastoma is not clear.[29] Most authors attribute its origin to striated muscle. Fust and Custer [30] were of the opinion that all myoblastomas are derived from nerves and not from skeletal muscle. This study needs confirmation. I have observed discrete lesions of myoblastoma that have occurred in the perineal region and on the labia, where no striated muscle is present. The granular cells in the tumors in this location apparently arose from the endothelium of the walls of the smaller capillaries, and the smooth muscles were not involved.

The histological picture of granular cell myoblastoma is distinctive. It usually is a circumscribed tumor composed of sheets and cords of large, irregular, round, oval or polygonal cells that have a poorly defined cellular membrane and acidophilic, coarsely granular cytoplasm. The cells may have a single vesicular nucleus but at times may be multinucleated. The resemblance of granular cells to xanthoma cells is striking, but stains for fat fail to reveal lipids. Granular cell myoblastoma rarely undergoes malignant change.[31] Treatment is surgical.

Granuloma Pyogenicum.—This entity needs only to be mentioned because, when it occurs in relation to the finger nails or elsewhere, it may be mistaken for malignant melanoma, in view of its dark-blue color and pedunculated appearance. On the other hand, actively growing melanomas that tend to bleed have been diagnosed erroneously as granuloma pyogenicum. Histological study is indicated.

Hemangiopericytoma.[32]—This tumor has no clinically distinctive features. It may occur as a cutaneous or subcutaneous tumor anywhere on the body and is characterized by the presence of so-called pericytes. Some workers see a close relation between hemangiopericytoma and glomus tumor. Metastasis and death occasionally occur.

This presentation merely will mention hemangioma, lymphangioma, synovial tumors, lipomas, and osteomas. These various tumors are described adequately in textbooks on dermatology and pathology.

MALIGNANT DERMAL NEOPLASMS

Following is a classification of malignant tumors of the skin.

- Dermatofibrosarcoma protuberans
- Kaposi's sarcoma
- Other sarcomas (including indeterminate)
  - Fibrosarcoma, angiosarcoma, myxosarcoma, liposarcoma, synovial sarcoma
  - Pleomorphic myoblastoma, rhabdomyosarcoma
- Melanosarcoma
- Hemangioendothelioma, lymphangiosarcoma, pericytoma
- Metastatic tumors
- Teratomas
- Miscellaneous (rarely involving the skin)

Transitions from benign to malignant dermal neoplasms sometimes occur after repeated irritation and trauma as in blue nevi.

Dermatofibrosarcoma Protuberans.—This lesion is of special interest to the dermatologist.[33] It is characterized by the presence of variably sized plaques and tumors with a predilection for the abdominal wall, thorax, and lower extremities, but it has been reported on the genitalia and head. The condition begins usually with several reddish to bluish pink nodules that increase in size and coalesce to form plaques of variable dimensions. The plaques may not be elevated in all cases. Some, however, become

pedunculated and ulcerate. The histological picture is that of a low grade fibrosarcoma. Large lacunar spaces may be seen, and later myxomatous and edematous changes may occur. Mitotic figures are relatively few, and often the histological picture simulates closely that of the histiocytomatous type of nodular epidermal fibrosis. Deposits of hemosiderin may be present. This may result in a bluish color, and the pigment may be mistaken for melanin if special stains are not done; hence an erroneous diagnosis both clinically and histologically has been made of malignant melanoma. I do not believe that dermatofibrosarcoma has a neural epithelial origin as some authors have maintained.

The condition is malignant locally and recurs frequently unless wide surgical excision is practiced. Pack and Tabah,[33b] in a review of 39 cases, stated, "if we were to judge the character of this neoplastic disease solely on the basis of our own experience, we would consider the title of dermatofibrosarcoma to be a misnomer because none of our patients has died of the disease or showed metastases." Binkley [33a] and Penner,[34] however, have recorded cases in which metastasis has occurred. In Penner's case, multiple local recurrences took place for a period of 28 years before death occurred. This case was of interest because the initial lesion started when the patient was 3 years of age. The condition usually appears after the age of 26 years.

This tumor should not be classified as primary fibrosarcoma of the skin, because the latter tumor, including those that start in the subcutaneous tissues and extend to the skin, often pursues a much more rapid and malignant course.

Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi.—This relatively rare tumor also is of special dermatological interest. It displays a fairly characteristic clinical picture, for which many new names have been given, depending on the concept of the histogenesis of the disease. The condition formerly was thought to occur especially among Russian and Polish Jews, but now it is known to be found in persons of any race or religion and of any country. About 90% of the lesions occur in men, usually those in the later decades. It has, however, been reported in children.

Kaposi's sarcoma begins usually on the hands or feet, but Dörffel [35] and Becker and Thatcher [36] have noted that it may start anywhere on the body. Early lesions appear as reddish brown or bluish nodules that vary from a few millimeters to a few centimeters in diameter. They may be discrete or grouped. The lesions appear often as bluish infiltrations without visible nodules. Later, infiltrated plaques appear, and hard, reddish swelling of the hands and feet may occur that results ultimately in elephantiasis. Purpuric, bullous lesions occur also, and a tendency is noted for gradual dissemination through the lymphatic vessels rather than the blood stream. Arthralgias and swelling of the extremities are common. Visceral involvement is present in about 10% of cases. It is questionable whether this represents metastasis or whether in some cases multiple primary lesions occur in the internal organs,[37] especially in the few cases in which cutaneous lesions have not appeared. The disease formerly was thought to pursue a rather rapid course, with death resulting as early as eight months after onset. The average duration before death apparently ranges from 5 to 10 years, although Dörffel [35] reported a case in which the disease lasted 25 years, at which time death occurred from an intercurrent infection. Other workers have reported survivals of 15 years or more.

A study has been made of some 35 cases of Kaposi's sarcoma encountered at the Mayo Clinic. In addition, I have studied material in some 20 outside cases and, in my opinion, the histological changes in this disease are essentially as worked out by Dörffel when he did the major part of his studies in my laboratory.

The initial histological picture in Kaposi's sarcoma is that of an inflammatory process rather than that of a neoplastic process. These histological changes make Kaposi's sarcoma distinctive from other sarcomas and also cause confusion in its histogenesis. The initial change results from hemorrhage in the cutis from one or more vessels that are dilated and engorged, and deposition of hemosiderin is present. The next change is a predominance of the lymphocytoid cells of Marchand, which apparently arise from the walls of the blood vessels. Later, proliferation of the endothelium of the blood vessels occurs, together with the formation of new but imperfect capillaries and an increase in lymphocytes, plasma cells, and mast cells. The so-called lymphocytoid cells later form spindle-like cells, and an increase in reticulum cells or fibroblasts, or both, also is present. After this stage, in which the histological picture resembles that of a cavernous hemangioma, the microscopic appearance definitely becomes that of angiosarcoma or fibrosarcoma. McCarthy and Pack,[38] as well as others who have done tissue cultures,[36] were of the opinion that the spindle-like cells more likely implicate a primitive mesenchymal tissue and that the cells are not of fibroblastic origin. However, in ordinary paraffin sections, distinction from a fibrosarcoma often is difficult.

One of the characteristics of Kaposi's sarcoma is that the early stage of inflammation and the later stage of tumor formation frequently may be seen in the same lesion, together with deposition of hemosiderin. An increasing number of reports of Kaposi's sarcoma are appearing in which the disease is associated with mycosis fungoides, Hodgkin's disease, or other forms of lymphoblastoma. This suggests some relationship to the reticuloendothelial system. Dörffel [35] and Flarer emphasized the presence of monocytic elements in the blood stream as well as in the tumors. McCarthy and Pack recently have grouped Kaposi's sarcoma with malignant tumors of blood vessels but separated it from angiosarcoma because of the more benign course and the rather characteristic clinical appearance of Kaposi's sarcoma.[38]

Despite the vascular proliferation and hemorrhagic lesions, it is probably a mistake to change the designation to Kaposi's hemangioma as has been done in the recent summary of standard nomenclature. Kaposi regarded the condition as a true blastoma and essentially a sarcoma. Others regarded it as a hamartoma and as a granuloma originating in neural tissue. This opinion has few supporters today. Becker [36] expressed the opinion that the

disease represented a multicentric benign neoplasm originating in perithelial tissue from embryonic mesenchymal cells (lymphocytoid cells of Marchand) and that after a period of years the cells underwent malignant degeneration, producing true sarcoma with resultant metastasis and death. Dörffel [35] emphasized the reticuloendothelial origin, although he would agree concerning the lymphocytoid cell. Some authors would classify Kaposi's sarcoma as hemangioendothelioma or as other vascular tumors, such as angioblastoma.[39] This is not too objectionable, although McCarthy and Pack pointed out that hemangioendothelioma is used loosely to designate both benign and malignant angiomatous tumors. Greco's concept of the disease as being of infectious fungal origin has not been substantiated.

Clinical diagnosis of Kaposi's sarcoma should be confirmed by histological studies in all cases, because circulatory disturbances, lymphoblastomas, chronic granulomas of the extremities, and true angiosarcomas in particular may simulate this tumor. The treatment of choice for Kaposi's sarcoma has been the use of roentgen rays. In one patient seen at the clinic, no recurrence was evident 12 years after roentgen therapy. As a rule, roentgen therapy merely is palliative, but its judicious use may prolong life for many years. Early reports of successful treatment with penicillin have been refuted.

Other Sarcomas.—As shown in the classification of malignant dermal neoplasms, the various types of sarcomas are dependent on the type of tissue involved, and different pathologists have presented various classifications, depending on whether emphasis is put on the type of tissue or the type of tumor.[40] Other tumors of soft tissues have been classified as neurogenic sarcomas, whether or not they have any relationship to neurofibromatosis, and still others have been designated as mesenchymomas. Recently, Christopherson and his associates [41] described alveolar sarcomas of soft tissues with structurally characteristic tumors of uncertain histogenesis. These tumors have no characteristic clinical picture and vary greatly in size and in prognostic potentialities. They usually begin in the subcutaneous tissues or muscles and involve the skin only secondarily. Most frequently they are of such size that they are seen by the surgeon rather than by the dermatologist.

Broders and his associates [42] have stated that fibrosarcomas and myosarcomas occur in persons older than those in whom spindle cell sarcomas, which pursue a more malignant course, occur. Fibrosarcomas may be graded in degree of malignancy just as are carcinomas. Liposarcomas and benign lipomas have been reviewed by Willis [43] and others.

Synovial sarcomas are rare tumors that occur on the extremities and are extremely malignant.[44]

Pleomorphic myoblastomas, according to Murphy and his associates,[28b] have granular cells in common with the benign uniform or granular cell type of myoblastoma, but the granules are larger and a more distinct cellular membrane is present than occurs in the uniform or granular type. The pleomorphic myoblastoma displays a spindle type stroma with scattered giant cells that are round, oval, or teardrop-shaped. The cells contain a large amount of granular cytoplasm, and numerous mitotic figures are noted in all types of cells. These authors regarded pleomorphic myoblastoma as closely related to, if not actually a form of, rhabdomyosarcoma. These tumors arise apparently from striated muscles. Dockerty and Broders [45] studied a case in which a uniform or granular cell myoblastoma of the labia underwent early malignant change of a pleomorphic type and was associated with a frank hemangioendothelioma. This again raises the question of whether the malignant as well as the benign types of myoblastoma and rhabdomyoma may have an endothelial or even a histocytic origin.

Melanosarcoma.—Strictly speaking, this term should apply only to malignant changes in a blue nevus. Since evidence is accumulating that blue nevus cells, in common with ordinary nevus cells, originate from the neural crest, melanosarcoma becomes a misnomer.

Hemangioendothelioma.[46]—This designation has been used at the clinic to apply to malignant vascular tumors, which have been classified according to the usual degrees of malignancy. Again, diagnosis cannot be made on a clinical basis alone. The skin of the face and eyelids frequently may be involved, but hemangioendothelioma can occur anywhere on the body. Combinations of hemangiolymphangiomas and sarcomas have been encountered.

Metastatic Tumors.—These may occur on the skin as the result of spread from almost any type of malignant growth anywhere in the body. The metastatic nodules occur usually in the upper or deeper portions of the cutis and as a rule do not involve the epidermis, except to cause atrophy from pressure. Most physicians are familiar with metastatic lesions from melanomas, adenocarcinomas of the gastrointestinal tract, and hypernephromas. I have encountered two unusual cases. One was that of a chordoma in which a direct extension to the skin over the sacrum resulted in an ulcerated and granulomatous mass. The second case was that of a massive meningioma that had produced erosion of the skull. A large tumor of the scalp was present, together with metastasis to the cervical lymph nodes. This case was reported by Laymon and Becker.[47]

In some cases, small cutaneous metastatic nodules may be present in the scalp or elsewhere before any clinical or laboratory evidence of a primary internal malignant neoplasm is present.[48] Recognition of these metastatic nodules and performance of a cutaneous biopsy may obviate an unnecessary exploratory operation.

SUMMARY

This presentation consists of a brief review of benign and malignant dermal neoplasms in which emphasis is placed on a few types. Histological study is necessary for correct diagnosis of these lesions, except for a few benign dermal neoplasms. The dermatologist should be familiar with the varieties of dermal neoplasms that usually are encountered by the surgeon and surgical pathologist. Conversely, the dermatologist and dermatohistopathologist can be of help to the clinician and pathologist, especially regarding the smaller cutaneous neoplasms.

THE POSTPARTUM CERVIX

John H. Moore, M.D.
and
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The cervix uteri does not receive the attention it deserves in the practice of obstetrics. It is a hidden and a neglected portion of the birth-canal; hidden, because the physician too often does not think it important to palpate it, much less to visualize it, and neglected for the foregoing reason as well as because its anatomic and physiological functions are taken too much for granted.

If the above statements are true, it is not surprising that pathological changes in the cervix, sometimes of major importance to the health and well-being of the child-bearing woman, can and do remain unrecognized for long periods of time. As obstetricians and gynecologists, we feel that treatment of the postpartum cervix should be considered in three phases: (1) antepartum appraisal of the cervix in both primiparous and multiparous patients; (2) inspection of the cervix immediately post partum and, in suitable cases, immediate repair; and (3) examination of the cervix at six weeks post partum, with careful reevaluation and subsequent treatment when indicated.

TABLE 1.—*Antepartum Cervical Abnormalities*

Lesion	Multiparas	Primiparas
Erosion, with or without eversion	62	15
Laceration	51	1
Cystic cervicitis	9	1
Polyps	3	0
Combined lesions	34	3
Previous cervical surgery	9	0
Total	168	20

The basis for this report is a series of 500 consecutive private obstetric patients who have been under our care in the department of obstetrics and gynecology of the Grand Forks Clinic. The series included 364 multiparous and 136 primiparous patients.

ANTEPARTUM APPRAISAL OF THE CERVIX

We believe that no prepartum examination is complete unless the cervix is palpated and visualized. Table 1 gives the results of such examinations in this series. There were no malignant growths, congenital malformations, or tumors other than polyps in this series. The combined lesions all showed lacerations and, in addition, erosion, infection, and/or polyp formation. Leukorrhea was the chief symptom in this group. It was present in 66 of the multiparous patients and 8 of the primiparous patients, or approximately 40%.

In this group of 188 patients, we felt that the antepartum cervical abnormalities discovered warranted treatment in 62, or 37%, of the multiparous and 10, or 50%, of the primiparous patients. The lesions of 40 of the 72 treated patients were cauterized. The remaining 32 patients were treated symptomatically with "triple sulfa cream" (sulfathiazole, *N'*acetylsulfanilamide, *N'*benzoylsulfanilamide and urea peroxide) or floraquin® (diiodohydroxyquinoline–U.S.P., lactose, dextrose, and boric acid) tablets.

In this group of 500 consecutive patients, there were only 29 abortions, an incidence of 5.8%. Twenty-two of these were in the multiparous and 7 in the primiparous group. In the 29 patients who aborted, cervical abnormalities were present in 8 of the multiparous and 2 of the primiparous patients. We treated the cervix in only three of the patients who subsequently aborted within six weeks of the cervical treatment.

TABLE 2.—*Cervical Lacerations at Delivery*

Type of Delivery	Multiparas	Primiparas
Spontaneous	20	4
Low forceps	16	15
Rotation and forceps delivery	12	3
Midplane forceps	4	2
Breech	6	0
Version and extraction	1	0
Abortions, spontaneous	2	0
Total	61	24

IMMEDIATE POSTPARTUM APPRAISAL OF THE CERVIX

We know of no way by which the condition of the cervix immediately following delivery can be determined except by actual visualization. We inspect every cervix immediately on the completion of the third stage of labor. As a result of this inspection, it was found necessary to repair surgically the cervix in 61 of the multiparous and 24 of the primiparous patients, or 17% of this series. We repair every cervix immediately postpartum in which we can recognize a laceration (table 2). We wish to call attention to the fact that 24 of the 85 cervical lacerations repaired immediately following delivery, or slightly over 28%, occurred following spontaneous deliveries.

The lacerations were bilateral in 68 and unilateral in 16 patients of this series. One laceration occurred posteriorly. Twenty-eight of the repairs were done on patients who had had previous lacerations. Fifty of the 85 patients in whom repairs were done had had previous cervical abnormalities. Thirty of the 85 patients did not have episiotomies, including 2 primiparous patients. The morbidity in the 85 patients was 10.5%. The over-all

TABLE 3.—*The Postpartum Cervix*

Lesion	Multiparas		Primiparas	
	Repaired	Not Repaired	Repaired	Not Repaired
Erosion, with or without eversion	16	89	15	48
Lacerations	3	10	0	4
Cystic cervicitis	0	3	0	0
Combined lesions	5	26	0	10
Total	24	128	15	62

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Read before the Section on Obstetrics and Gynecology at the 101st Annual Session of the American Medical Association, Chicago, June 10, 1952.

morbidity for the entire series was 7.4%. We found no evidence of pelvic infection or hemorrhage due to cervical repair. Antibiotic or sulfone therapy was not used prophylactically.

APPRAISAL OF THE CERVIX AT SIX WEEKS POST PARTUM

Since it has not been difficult to convince our patients of the importance of postpartum care, we have had an excellent follow-up. When the patients return for their six weeks postpartum examination, it goes without saying that the cervix in all of them is critically appraised. Table 3 gives the results of this appraisal.

There were 229 cervices showing postpartum lesions in the entire series of 500 patients. It was very revealing to us that, in spite of antepartum care of the cervix and immediate postdelivery repair in a substantial number of the patients of this series, 229 patients still had cervical abnormalities at six weeks post partum. This included 72 who had had antepartum treatment and 85 in whom repair had been done immediately after delivery, or a total of 157 of the 229 patients. Of this number, 207 were treated by cautery and surgery was advised for 22. We do not wish to leave the impression that the care of the postpartum cervix ceases with the six weeks appraisal of it. Every pathological cervix should be followed.

COMMENT

In this series of cases we have called attention to the importance of the cervix during three phases of the obstetric cycle. In the antepartum period a high incidence of cervical abnormality will be found if one looks for it. In our series the incidence of antepartum cervical lesions was 37%. Likewise, at the time of delivery we found it necessary to immediately repair 17%. At the six weeks appraisal of the postpartum cervix we still found that the cervices of 46% of the 500 patients in this series required treatment. One observation will illustrate this point: In spite of the fact that we did immediate postdelivery repair on 85 cervices, there were 22 additional patients in whom surgical repair of the cervix was advised at the postpartum checkup. Our judgment must have been faulty in that we did not recognize the need for repair at the time of delivery. This has been a factual presentation of what we have found in a series of private obstetric patients, and it has been presented with the hope that it will focus more attention upon an organ that does not receive enough surveillance during the reproductive period.

SUMMARY AND CONCLUSIONS

Five hundred consecutive private obstetric patients from the department of obstetrics and gynecology of the Grand Forks Clinic have been studied as to cervical abnormality. While diligent search for and attempted correction of cervical abnormalities was carried out in the prepartum and postpartum phases of our obstetric care of these patients, the cervices of 229 of these 500 patients, or 46%, failed to meet our standards. We urge antepartum treatment of the cervix, immediate postdelivery repair, and subsequent complete follow-up. The series of cases presented is admittedly small. It would be desirable to study and evaluate much larger series of cases in order to repudiate or validate our findings.

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FURTHER EXPERIENCE WITH COUMARIN ANTICOAGULANTS

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and
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Bishydroxycoumarin (dicumarol®), cyclocumarol* ("cumopyran"), and ethyl biscoumacetate (tromexan®) are 4-hydroxycoumarin derivatives that have been used as anticoagulants in the treatment of thromboembolic diseases. Their therapeutic action depends on depression of the prothrombin activity of the blood, and frequent prothrombin determinations are necessary for their adequate control. Our aim has been to find a safe anticoagulant that is prompt in its therapeutic action and that produces hypoprothrombinemia of such regularity and similar degree that the frequency of prothrombin determinations could be lessened. A comparison of the chemical formulas of these three compounds was shown in the papers of Barker, Hanson, and Mann[1] and Shapiro.[2] The similarity was apparent from the presence of the 4-hydroxycoumarin radical in each. Cyclocumarol is about 1/100 as soluble in water as bishydroxycoumarin, while ethyl biscoumacetate is more soluble than bishydroxycoumarin. On a milligram per kilogram of body weight basis, cyclocumarol is about two and one-half times more potent than bishydroxycoumarin, while ethyl biscoumacetate is only about one-fifth to one-sixth as potent as bishydroxycoumarin.

A comparison of usual dosages of the coumarin anticoagulants is given in the table. The initial dose of bishydroxycoumarin is 5 mg. per kilogram of body weight, and the average daily maintenance dose is 1.5 mg. per kilogram of body weight, although it depends on the prothrombin time for each day. For cyclocumarol, a dose of 2 mg. per kilogram of body weight is required initially, while from 0.5 to 1 mg. per kilogram is usually needed daily to maintain therapeutic hypoprothrombinemia. The proper initial dose of ethyl biscoumacetate is 1,200 to 1,500 mg., and from 300 to 600 mg. are required daily for maintenance therapy. In all instances,

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* This is the generic name for the compound previously reported under the name 4-hydroxycoumarin anticoagulant no. 63.

1. Barker, N. W.; Hanson, H. H., and Mann, F. D.: Bishydroxycoumarin, Ethyl Biscoumacetate, and 4-Hydroxycoumarin Anticoagulant No. 63, J. A. M. A. **148**: 274 (Jan. 26) 1952.

2. Shapiro, S.: The Management of Oral Anticoagulant Therapy, Postgrad. Med. **11**: 73 (Jan.) 1952.

frequent prothrombin determinations are required. The maintenance dose depends on the prothrombin time for that day and on whether the value is falling or rising.

Determinations of prothrombin time were done on 100% plasma by the one stage method of Quick,[3] using Difco thromboplastin. The optimum calcium concentration recommended by Stewart and Pohle [4] was employed. For each patient, all prothrombin studies were performed daily by the same technician at about the same time. Control prothrombin times varied between 11 and 13 seconds, and results were reported in percentages of normal. With a 12 second control, 100% = 12 seconds, 80% = 13 seconds, 60% = 14 seconds, 40% = 17 seconds, 20% = 25 seconds, and 10% = 42 seconds. An attempt was made to keep the values between 20 and 40% of normal as a probable satisfactory therapeutic range. In all cases, a base line prothrombin time was determined, and no anticoagulant was administered unless the value was at least 70%.

patients was subsequently maintained at a therapeutic level with cyclocumarol without difficulty.

Since our initial report, cyclocumarol has been administered to two persons on an outpatient basis for over six months. One patient, a 55-year-old white man, received a six week course of cyclocumarol when he had acute myocardial infarction in April, 1951. He was again hospitalized in September, 1951, and treated for recurrent infarction during another six week period. Since his discharge in November, 1951, he has been maintained on 25 mg. of the anticoagulant every other day up to the time of writing. During this period, he has had prothrombin determinations made about once each week, and most of the prothrombin values have been within the therapeutic range. By June 1, 1952, he had received a total of 3,650 mg. of the anticoagulant. The other patient, a 62-year-old white woman, was treated with cyclocumarol for acute myocardial infarction in July, 1951. After her discharge from the hospital, she began to experience repeated attacks of coronary insufficiency. In the hope of preventing future episodes of coronary thrombosis, the patient was placed on maintenance cyclocumarol therapy. Since November, 1951, the patient has taken 50 mg. of the anticoagulant each day. At the time of writing, she was reporting for prothrombin time determinations once a week, and almost all the values were well within the therapeutic range of 20 to 40%. On one occasion, the patient had a small subconjunctival hemorrhage, but, despite continued anticoagulant therapy, the hemorrhagic area rapidly returned to

Comparison of the Coumarin Anticoagulants

	Chemical Name	Comparative Solubility in Water	Comparative Potency Mg. for Mg.	Initial Dose	Average Daily Maintenance Dose	Latent Period, Hr.	Approximate Time Required to Produce Therapeutic Hypoprothrombinemia, Hr.	Average Time Required for Prothrombin Level to Return to Normal After Single Dose, Days	Antidotes
Bishydroxycoumarin	3,3'-methylenebis (4-hydroxycoumarin)	1 *	1 *	5 mg./kg.	1.5 mg./kg.	24	48 to 72	4	(1) Fresh blood transfusion; (2) water soluble vitamin K; (3) vitamin K_1 and vitamin K_1 oxide, probably better than (2)
Cyclocumarol	2-methyl-2-methoxy-4-phenyl-5-oxodihydropyrano-(3,2-c) benzopyran	1/100	2 to 3	2 mg./kg.	0.5 to 1.0	18 to 24	24 to 48	8	(1) Vitamin K_1 and vitamin K_1 oxide; (2) water soluble vitamin K, far less effective than (1); (3) blood transfusion (ineffective in our experience)
Ethyl Biscoumacetate	3,3'-carboxymethylenebis-(4-hydroxycoumarin) ethyl ester	>1	1/5 to 1/6	1,200 to 1,500 mg.	300 to 600 mg.	8 to 12	18 to 36	1 to 2	Antidotes difficult to assess because of spontaneous prompt return of prothrombin to normal

* Indicates unity, for sake of comparison.

CYCLOCUMAROL

To date, cyclocumarol has been administered to over 200 patients at the University Hospitals, Madison, Wis. In general, our continued experience tends to bear out the original impression that cyclocumarol is capable of producing therapeutic hypoprothrombinemia more rapidly than does bishydroxycoumarin and that it permits easier maintenance of a satisfactory prothrombin level with a relatively fixed dose of the drug.[5] In 78% of the patients treated, a prothrombin value of 40% or less within 48 hours after the administration of an initial dose of cyclocumarol can be anticipated. Similar results with cyclocumarol have been obtained by Hanson, Barker, and Mann.[6] They also showed that this preparation was capable of inducing adequate hypoprothrombinemia within 48 hours after the first dose had been given in five patients who showed resistance to bishydroxycoumarin. In this group, the use of bishydroxycoumarin in fairly large doses had failed to prolong the prothrombin time into the therapeutic range. Prothrombin time in these

3. Quick, A. J.: The Nature of Bleeding in Jaundice, J. A. M. A. **110**: 1658 (May 14) 1938.

4. Stewart, J. K., and Pohle, F. J.: Effect of Calcium in Quantitative Determination of Prothrombin, Proc. Soc. Exper. Biol. & Med. **39**: 532 (Dec.) 1938.

5. (*a*) Rotter, R., and Meyer, O. O.: Clinical Evaluation of 4-Hydroxycoumarin Anticoagulant No. 63, J. Lab. & Clin. Med. **36**: 981 (Dec.) 1950. (*b*) Rotter, R., and Meyer, O. O.: Clinical Evaluation of 4-Hydroxycoumarin Anticoagulant No. 63, A. M. A. Arch. Int. Med. **88**: 296 (Sept.) 1951.

6. Hanson, H. H.; Barker, N. W., and Mann, F. D.: Clinical Experiences with 4-Hydroxycoumarin Anticoagulant No. 63 and the Antagonistic Effect of Menadione and Vitamin K_1, Circulation **4**: 844 (Dec.) 1951.

normal. By June 1, 1952, this patient had received a total of 9,650 mg. of the anticoagulant.

Since our initial report on our clinical experience with cyclocumarol, we have observed a toxic response in another patient who inadvertently received an overdose of the drug. This patient was a 61-year-old white man with arteriolar nephrosclerosis and uremia, who was treated with this anticoagulant because of the development of pulmonary infarction. By mistake, the prothrombin time determinations were made on blood taken from another patient with the same name. When subcutaneous bleeding developed at the site of hypodermocylsis needles in the patient receiving the anticoagulant, the error was realized and he was treated with vitamin K_1 and a blood transfusion. There was a prompt return of the prothrombin level to normal, but the patient died two weeks later. An autopsy revealed the presence of a hemorrhagic pericarditis as well as arteriolar nephrosclerosis. While it is entirely possible that uremia could explain the hemorrhagic manifestations, the anticoagulant perhaps contributed somewhat. Thus, hemorrhagic side-effects attributable in part to cyclocumarol have now been observed in only 5 of the more than 200 patients who have received it.

In general, our further experience with antidotes for hypoprothrombinemia induced by cyclocumarol confirms our initial impression that large doses of vitamin K_1 or vitamin K_1 oxide given orally or intravenously are the most efficacious agents.[5b] The water soluble vitamin K preparations are far less effective in the case of a bleeding emergency. Shapiro,[7] on the other hand, believes that administration of large doses of fresh blood results in a prompt reduction in excessive hypoprothrombinemia in a manner indistinguishable from that observed after fresh blood has been administered to a patient with bishydroxycoumarin-induced hypoprothrombinemia.

We have seen only one instance of resistance to vitamin K_1. The patient was a 52-year-old white man who was being treated with cyclocumarol because of the development of a popliteal embolus. When the prothrombin level fell to 18%, the patient was given 100 mg. of emulsified vitamin K_1 intravenously. In four hours the prothrombin level was 23%, and another 100 mg. of this antidote was administered. Twenty hours later the prothrombin level was 45%, but another 100 mg. failed to alter this value in 24 hours. Then 1 gm. of vitamin K_1 was given orally, but after 24 hours the prothrombin value was still 45%. Another gram of vitamin K_1 given orally increased the prothrombin level to 52%. This value remained the same with no further therapy for three days, after which the patient died of migrating visceral thrombophlebitis.

ETHYL BISCOUMACETATE

The first reported synthesis of this compound was carried out by Reinîs and Kubik in 1948.[8] Its relative solubility, potency, and dosage are given in the table. After the administration of an initial dose of 1,200 to 1,500 mg., there is a latent period of 8 to 12 hours, and therapeutic hypoprothrombinemia is usually apparent in 18 to 36 hours. The average maintenance dose is 300 to 600 mg. per day, depending on the prothrombin time. Usually, only 24 to 48 hours are required for the prothrombin level to return to normal after maximum hypoprothrombinemia has been produced by a single dose of this drug.

Ethyl biscoumacetate has been administered to 38 patients at the University Hospitals. Of this number, 13 received this anticoagulant exclusively and were maintained for from 6 to 38 days on this therapy. In one patient therapy was changed from cyclocumarol to ethyl biscoumacetate after therapeutic hypoprothrombinemia had been attained. The remaining 24 patients were given this drug in conjunction with cyclocumarol. In 10 (76.9%) of the 13 patients who received ethyl biscoumacetate exclusively, the prothrombin time fell to the therapeutic level (20 to 40%) in 24 hours. In an additional two patients (15.4%) it reached the therapeutic level in 48 hours, and in one (7.7%) 72 hours were required to attain this level. In 6 of the 24 patients who received combined therapy with ethyl biscoumacetate and cyclocumarol, hypoprothrombinemia was induced with ethyl biscoumacetate and was then maintained with cyclocumarol. In four of these the prothrombin level went below 40% in 24 hours; in the remaining two this required 48 hours. Of the 16 patients who were treated initially with the combined anticoagulants, 7 (43.8%) required 24 hours and 9 (56.2%) required 48 hours to attain therapeutic hypoprothrombinemia. Two patients received suboptimal doses of the combined anticoagulants, and 48 hours were needed for the prothrombin time to reach an adequate level. These results indicate that ethyl biscoumacetate acts more rapidly than both cyclocumarol and bishydroxycoumarin.

The chief disadvantage of ethyl biscoumacetate is its inability to maintain a stable level of hypoprothrombinemia when given in a fixed single daily dose. This compound is so rapidly metabolized that failure to administer it for one day is associated with a rapid return of the prothrombin time toward normal. This difficulty in maintaining patients on ethyl biscoumacetate is illustrated in the figure. In this patient, an initial dose of 1,200 mg. produced prothrombin times of 40% and 27% in 18 and 24 hours, respectively. When the prothrombin time fell below 20%, it was thought to be unsafe to administer more anticoagulant. Omission of the drug was associated with a sharp return of the prothrombin time to 77% in 24 hours. This same phenomenon was observed later in the course of therapy in this patient and in other patients as well. The experience of Barker, Estes, and Mann has been similar.[9] With the administration of smaller doses of ethyl biscoumacetate when the prothrombin time is in a critically low range, greater uniformity of control may be obtained, but, at the same time, the danger of hemorrhage is increased.

We observed only one instance of resistance to ethyl biscoumacetate in our series. This patient was a 38-year-old white man who was receiving an anticoagulant because of the development of a popliteal embolus. A total of 3,900 mg. was required to induce therapeutic hypoprothrombinemia in 96 hours, and the patient was sub-

7. Shapiro, S.: The Hypoprothrombinemia-Inducing Activity of Link's Compound No. 63 (Methopyranorin), Acta haemat. **6**: 129 (Sept.) 1951.

8. Reinîs, Z., and Kubik, M.: Klinische Erfahrungen mit einen neuen Präparat der Cumarinreihe, Schweiz. med. Wchnschr. **78**: 785 (Aug. 14) 1948.

9. Barker, N. W.; Estes, J. E., Jr., and Mann, F. D.: Clinical Experiences with the Anticoagulant, Ethyl Biscoumacetate (N.N.R.), Proc. Staff Meet., Mayo Clin. **26**: 162 (April 25) 1951.

sequently not maintained at the proper prothrombin level with as much as 1,350 mg. per day. When the therapy was changed to cyclocumarol, adequate hypoprothrombinemia was readily induced and maintained with 50 mg. per day.

Only one instance of hemorrhage possibly attributable to this anticoagulant was observed. This occurred in an elderly man who was recuperating from a transurethral prostatectomy. The anticoagulant was administered because of the development of thrombophlebitis, and bleeding occurred through a retention catheter at a time when the patient's prothrombin level was 34%. The bleeding stopped within 24 hours after the administration of a blood transfusion. Whether the blood loss was due to the alteration in clotting mechanism induced by the anticoagulant is difficult to say, since the trauma of surgery may well have been responsible. It is believed, however, that hypoprothrombinemia was at least a contributory factor.

The effectiveness of antidotes for the hypothrombinemia induced by ethyl biscoumacetate is difficult to assess, because mere omission of the anticoagulant is followed by a prompt return of the prothrombin level toward normal. It is the impression of Barker, Hanson, and Mann [1] that the use of menadione sodium bisulfite accelerates slightly the return of the prothrombin time to normal, especially if the prothrombin level is below the therapeutic range. They question whether vitamin K_1 is more effective when given orally, but they feel that it may be slightly more potent as an antagonist for ethyl biscoumacetate when given intravenously.

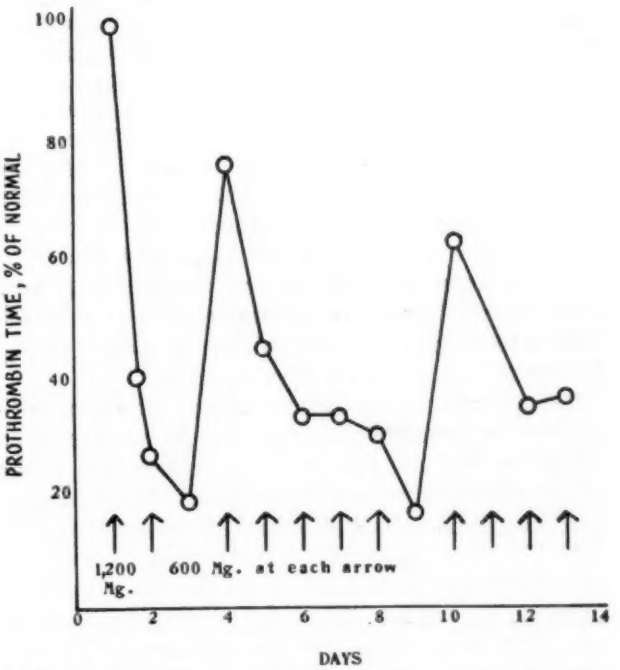
COMBINED COUMARIN ANTICOAGULANTS

In an attempt to combine the rapid action of ethyl biscoumacetate with the stable maintenance effect of cyclocumarol, these two anticoagulants were administered together in 24 patients. Initially, we attempted to induce adequate hypoprothrombinemia with ethyl biscoumacetate and then to maintain it by administration of cyclocumarol. Since the duration of action of ethyl biscoumacetate was so short and since there was usually a lag of 48 hours before cyclocumarol had its maximum effect, the prothrombin level usually "escaped" toward normal before smooth maintenance could be established. Consequently, this method was soon abandoned.

Our most recent approach has been to combine the anticoagulants in an initial dose, thus obviating the irregular response that occurred with the earlier method. The dose schedule adopted was as follows: 1. On the first day the patient is given 1,200 mg. of ethyl biscoumacetate with 50 mg. of cyclocumarol. 2. No additional ethyl biscoumacetate is administered. More cyclocumarol is given on the second day in a dose, determined according to the method previously outlined,[5b] that depends on the prothrombin time for that day. (If the prothrombin level is between 20 and 40%, 25 mg. are given; if the level is over 40%, 50 mg. are given; and if it is below 20%, none is given.) 3. Subsequent dosage of cyclocumarol depends on each day's prothrombin time and whether it is rising or falling. With this regimen, the prothrombin time in about half the patients treated had reached the therapeutic range in 24 hours, and in the remainder it had reached a proper level in 48 hours. This proved to be a prompt and efficient method for initiating and maintaining anticoagulant therapy. It is possible, of course, to obtain an even more rapid anticoagulant effect by administering heparin sodium initially and then maintaining therapy with cyclocumarol; however, this method has the disadvantage of necessitating multiple or continuous intravenous injections or intramuscular injections of an expensive drug.

COMMENT

The entire subject of anticoagulant therapy has become quite confused because of a lack of uniform terminology and a failure to establish criteria of good treatment. In the first place, there has been no unanimity in the reporting of prothrombin times. Many institutions report all results in seconds and compare the value to a normal control. We convert all values to a percentage of normal on the basis of a graph that plots the concentration of prothrombin in the plasma against the clotting time in seconds. This scheme gives a uniform basis for comparison of results obtained at various institutions.



Effect of administration of ethyl biscoumacetate on prothrombin time in a 34-year-old white man with thrombophlebitis.

What constitutes a "therapeutic" level of hypoprothrombinemia is another moot question. Using the original one stage method of Quick on undiluted plasma and employing an isotonic sodium chloride solution extract of dried rabbit brain as thromboplastin, the Mayo Clinic group [1] found that the normal prothrombin time for hospital patients is 18 to 20 seconds. Their arbitrary therapeutic range of hypoprothrombinemia induced by administration of a coumarin compound is considered to be between 27 and 58 seconds. Using the percentage method of reporting our results, we have arbitrarily considered the values of 20 to 40% (25 to 17 seconds, with a 12 second control) as a probable satisfactory therapeutic range. The ideal degree of hypoprothrombinemia is that level at which thrombotic episodes could not occur and yet spontaneous hemorrhage would be rare. Such a value is

difficult to determine and probably varies somewhat from one person to another.

According to Shapiro,[7] there are two methods for oral administration of anticoagulants, the maintenance method and the intermittent method. In the maintenance method, a larger dose is given initially and a smaller dose is given daily thereafter in an attempt to achieve and maintain a constant level of hypoprothrombinemia within a range believed to be safe and effective therapeutically. Shapiro has criticized this method as taking into account only the hypoprothrombinemia of the moment, with no consideration given to the question of whether the prothrombin time is rising or falling. In the second method, relatively large doses of hypoprothrombinemia inducing agents are given intermittently. A single effective initial dose is administered, and after the point of maximum prolongation of the prothrombin time has passed and recovery toward normal is occurring, a second effective dose is given. Shapiro claims that the intermittent dose schedule prevents accumulation of a slow acting drug in the body and permits full control of the anticoagulant effect. It is our opinion that these methods are not mutually exclusive, and we ordinarily combine some features of both in controlling anticoagulant therapy. Whenever we administer the drug, we take into account not only the prothrombin time for that day but also whether the value is rising or falling. Many of our patients receive the anticoagulant every other day or every third day, depending on the particular situation. Our aim is to find a pattern for uniform administration of an anticoagulant. In some patients, a small daily dose best satisfies the need; in others, the intermittent method is more valuable.

There is controversy over the criteria for a good antidote for the coumarin anticoagulants. As we have stated previously,[5b] in our opinion, mere prolongation of the prothrombin time beyond the therapeutic range does not constitute an immediate indication for the use of an antidote. The chief indications include the earliest sign of gross bleeding or the necessity for an emergency operation while the patient has drug-induced hypoprothrombinemia. With these criteria, the best antidotes for cyclocumarol and bishydroxycoumarin appear to be vitamin K_1 and vitamin K_1 oxide.[10]

While bishydroxycoumarin, cyclocumarol, and ethyl biscoumacetate are chemically related anticoagulants and probably have a similar mode of action, each has its own solubility and potency and, therefore, produces a different response in a given subject. Although bishydroxycoumarin has been used most extensively, cyclocumarol and ethyl biscoumacetate have the advantage of earlier onset of action, and cyclocumarol has the added advantage of producing relatively stable degrees of hypoprothrombinemia when administered in fixed doses.

It is possible that the ideal anticoagulant characterized by Shapiro and Weiner [11] may not prove to be a single compound. Combined anticoagulant therapy is not a new idea. Heparin has been used with bishydroxycoumarin for the purpose of producing and maintaining the blood in a hypocoagulable state during the latent period of action of the coumarin compound. Shapiro [7] observed that various combinations of the coumarin anticoagulants were consistently effective in 14 patients who received this form of therapy. Cyclocumarol was used in all the combinations that proved most effective. In our experience, by combining ethyl biscoumacetate, with its rapid action, with cyclocumarol, with its stable maintenance effect, we seem to be one step closer to having an ideal anticoagulant. By having more than a single anticoagulant available for clinical use, the physician is better equipped to cope with the problem of resistance and intolerance to a drug. Five patients who were resistant to large doses of bishydroxycoumarin responded well to cyclocumarol,[6] and we have observed an instance of resistance to ethyl biscoumacetate in which cyclocumarol proved effective. In Shapiro's experience,[7] it is unusual to find a subject who fails to respond to all these drugs.

Barker, Hanson, and Mann have stated [1] that if comparable degrees of therapeutic hypoprothrombinemia are established and maintained, these three coumarin compounds will probably be equally effective in preventing thrombosis, and their use will be attended by the same small risk of bleeding. In general, we would agree with this; but, from our experiences with cyclocumarol, we believe that the incidence of microscopic hematuria is less than that observed with bishydroxycoumarin.[5b] This may in part be related to a difference in the effect of large doses of these drugs on the blood vascular system.

To be able to eliminate entirely the necessity of prothrombin time determinations would be ideal, but this is impossible with any of the known coumarin anticoagulants or combinations thereof. Newer preparations show great promise in laboratory animals, but extensive clinical observation will be necessary before their value can be determined. In the meantime, we believe that the coumarin anticoagulants, either alone or in combination, provide good treatment for many thromboembolic disorders.

SUMMARY

Bishydroxycoumarin (dicumarol®), cyclocumarol ("cumopyran"), and ethyl biscoumacetate (tromexan®) are potent hypoprothrombinemic agents that have been used clinically in the treatment of thromboembolic disorders. Although bishydroxycoumarin has been used most extensively, ethyl biscoumacetate has the advantage of an earlier onset of action, and cyclocumarol is capable of producing greater stability in the degree of hypoprothrombinemia with a fixed dose of the drug. By combining the early action of ethyl biscoumacetate with the stable maintenance effect of cyclocumarol, satisfactory anticoagulant treatment can be instituted and maintained. The recommended dose schedule for the combined therapy is outlined. Resistance to one of the coumarin anticoagulants does not necessarily imply resistance to another. Therapeutic hypoprothrombinemia has been induced and maintained by cyclocumarol in patients who failed to respond to bishydroxycoumarin and ethyl biscoumacetate. With careful control, hemorrhagic side effects of the coumarin anticoagulants should be minimal.

10. Rotter and Meyer.[5b] James, D. F.; Bennett, I. L.; Scheinberg, P., and Butler, J. J.: Clinical Studies on Dicumarol Hypoprothrombinemia and Vitamin K Preparations: I. Superiority of Vitamin K_1 Oxide over Menadione Sodium Bisulfite U. S. P. and Synkayvite® in Reversing Dicoumarol Hypoprothrombinemia, Arch. Int. Med. **83**: 632 (June) 1949.

11. Shapiro, S., and Weiner, M.: Dicumarol Therapy, J. M. Soc. New Jersey **48**: 52 (Feb.) 1951.

PLATELET TRANSFUSIONS AND THE PATHOGENESIS OF IDIOPATHIC THROMBOCYTOPENIC PURPURA

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Interest in thrombocytopenic purpura has recently been stimulated by the demonstration that a circulating thrombocytopenic factor, presumably an antibody, is frequently involved in the pathogenesis of idiopathic thrombocytopenic purpura,[1] and by the suggestion that platelet transfusions may occasionally provide temporary relief from hemorrhagic manifestations in patients with low platelet levels caused by bone marrow depression.[2] During the past year, additional evidence has been obtained to indicate the importance of immunologic antiplatelet factors in the production of idiopathic thrombocytopenic purpura. It is the purpose of this paper to review that evidence, to relate it to previous ideas of pathogenesis, and to discuss the possible therapeutic application of platelet transfusions.

PATHOGENESIS OF IDIOPATHIC THROMBOCYTOPENIC PURPURA

The diminished number of platelets in idiopathic thrombocytopenic purpura has been attributed either to a decrease in their production or to an increased rate of destruction. Frank [3] was the first investigator to champion the former view, when he suggested that maturation of megakaryocytes became arrested, possibly by a factor produced by the spleen. This concept received support from the demonstration that an extract prepared from the spleen of a patient with idiopathic thrombocytopenic purpura injured megakaryocytes in bone marrow cultures.[4] In addition, Tocantins and Stewart [5] observed marked degenerative changes in megakaryocytes during the acute stage of experimental thrombocytopenic purpura in dogs. Then Dameshek and Miller,[6] in a study of bone marrow from patients with acute idiopathic thrombocytopenic purpura, stated that, while the total number of megakaryocytes was increased over normal values, the great majority of cells did not seem to be making platelets. Following splenectomy, a much higher percentage of the megakaryocytes showed evidence of platelet production. Not all investigators, however, have been willing to accept the morphological changes described by Dameshek and Miller as evidence of decreased platelet formation.

The theory of excessive destruction of platelets by the spleen and reticuloendothelial system was suggested by Kaznelson in 1916.[7] Wiseman, Doan and Wilson,[8] in support of this concept, have suggested that platelets are removed at an abnormal rate in the spleen, and they have found higher platelet counts in the splenic artery than in the splenic vein. Unfortunately, these observations have not been confirmed by all investigators. The difficulty in detecting statistically significant decreases in platelet counts produced during a single circulation through the spleen becomes apparent, however, from the fact that it usually takes several hours before transfused platelets disappear from the circulation of patients with acute idiopathic thrombocytopenic purpura. If all of the transfused platelets were removed by the spleen, the difference in splenic arterial and venous blood at any one time during the removal period would be difficult to measure, even with the most exact counting methods. The obvious criticism of this mechanism as an explanation of all types of idiopathic thrombocytopenic purpura is that a significant number of patients fail to respond to splenectomy. Proponents of the theory explain these failures on the basis of accessory splenic tissue or generalized reticuloendothelial hyperplasia, which takes over the platelet-removal function of the spleen.

The suggestion has also been made repeatedly that a capillary defect is of importance in the pathogenesis of idiopathic thrombocytopenic purpura. It has been postulated that such a defect would permit platelets to "leak out" of the circulation, so that thrombocytopenia would result. Bedson,[9] however, has shown that thrombocytopenia may be produced in experimental animals by the injection of agar-serum without the development of bleeding. Purpura did not occur unless he also injected an "anti-red cell serum," large amounts of which overwhelmed the protection. These observations have been confirmed by other workers.[10] It is difficult, on the basis of the leakage concept, to explain the temporary reversal of the hemorrhagic manifestations of idiopathic thrombocytopenic purpura that sometimes follows platelet transfusions.[2] Robson,[11] accepting the idea that the megakaryocyte develops extravascularly so that all or part of

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Because of lack of space some of the bibliographic references have been omitted from THE JOURNAL; they will appear in the authors' reprints.

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1. Harrington, W. J.; Minnich, V., Hollingsworth, J. W.; and Moore, C. V.: Demonstration of a Thrombocytopenic Factor in the Blood of Patients with Idiopathic Thrombocytopenic Purpura, J. Lab. & Clin. Med. **38**: 1, 1951.

2. Hirsch, E. O., and Gardner, F. H.: The Transfusion of Human Blood Platelets, J. Lab. & Clin. Med. **39**: 556, 1952. Stefanini, M.; Chatterjea, J. B.; Dameshek, W.; Zannos, L., and Santiago, E. P.: Studies on Platelets: II. The Effect of Transfusion of Platelet-rich Polycythemic Blood on the Platelets and Hemostatic Function in "Idiopathic" and Secondary Thrombocytopenic Purpura, Blood **7**: 53, 1952.

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6. Dameshek, W. and Miller, E. B.: The Megakaryocytes in Idiopathic Thrombocytopenic Purpura, a Form of Hypersplenism, Blood **1**: 27, 1946.

7. Kaznelson, P.: Verschwinden der hämorrhagischen Diathese bei einem Falle von essentieller Thrombopenie (Frank) nach Milzextirpation, Wien, klin. Wchnschr. **29**: 1451, 1916.

8. Wiseman, B. K., Doan, C. A. and Wilson, S. J.: The Present Status of Thrombocytopenic Purpura: With Special Reference to Diagnosis and Treatment, J. A. M. A. **115**: 8 (July 6) 1940

9. Bedson, S. P.: Blood-Platelet Anti-Serum, its Specificity and Rôle in the Experimental Production of Purpura, J. Path. & Bact. **25**: 94, 1922.

the cells must penetrate the intersinusoidal capillary wall in order to deliver platelets to the blood stream, believes that the altered state of capillaries in the bone marrow may prevent the delivery of adequate numbers of platelets to the circulation. Macfarlane [12] provided the most direct evidence for abnormal capillary function when he observed microscopically that the capillaries in idiopathic thrombocytopenic purpura were distorted and failed to contract normally when injured. Humble [13] localized the site of this defect to the arteriolar end of the capillary loop. The importance of a capillary defect cannot be minimized, because there frequently is poor correlation between the platelet level and the presence or absence of hemorrhage, but the factors responsible for the capillary defect and its exact nature are poorly understood.

No one of these concepts provides a complete explanation of idiopathic thrombocytopenic purpura. The studies that have demonstrated the presence of a circulating antiplatelet substance in many patients with the disease, however, have suggested that the three factors of increased platelet destruction, decreased platelet production, and a capillary abnormality may at times all be involved.

Evidence of a Circulating Thrombocytopenic Factor.—When 250 cc. of plasma or 500 cc. of whole blood from a patient with idiopathic thrombocytopenic purpura are injected into a normal recipient, frequently there is a

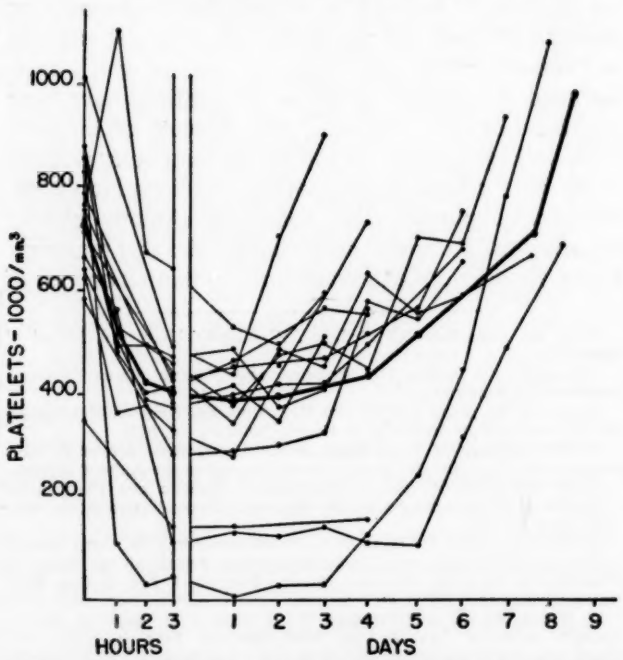

Fig. 1.—Decrease in the platelet count (indirect method) of recipients receiving either 500 cc. of whole blood or 250 cc. of plasma from patients with idiopathic thrombocytopenic purpura.

prompt, dramatic fall in the platelet count of the recipient. The fall occurs within the first three or four hours and persists for four to six days.[1] This effect has now been observed with the blood from 14 out of 18 patients with idiopathic thrombocytopenic purpura (fig. 1). At times the platelet level in the recipient has decreased to such low levels that the recipient had petechiae, increased capillary fragility, prolonged bleeding time, decreased prothrombin consumption, and even

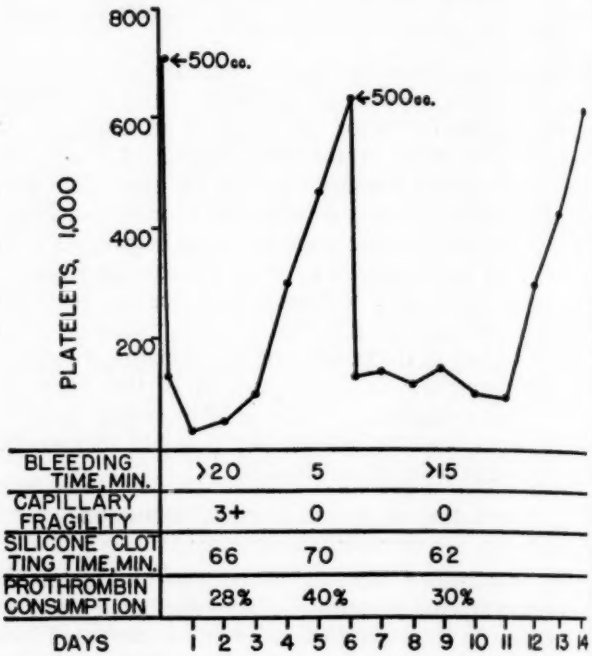

Fig. 2.—When 500 cc. of whole blood from a patient with idiopathic thrombocytopenic purpura was transfused into a normal recipient, there was a fall in platelet count, prolongation of the bleeding time, increased capillary fragility, and decreased prothrombin consumption. These results returned to normal over a period of five days, at which time a second transfusion was given with identical results except that the capillary fragility remained normal. As anticipated, the silicone clotting time was not altered by either transfusion. Reprinted with permission of the *Journal of Laboratory and Clinical Medicine*.

hemorrhage from the gastrointestinal tract (fig. 2). The thrombocytopenia that results is to be differentiated sharply from the very transient decrease in platelets that may occur during the first few hours after the transfusion of normal blood.[14] It has not been possible to demonstrate the thrombocytopenic factor in the blood of all adult patients with idiopathic thrombocytopenic purpura nor in the blood of most children with the disease.[15] The thrombocytopenic factor is stable at 4 C and 25 C for at least nine days, and seems to be associated with the globulin fraction of plasma.

Since transfused platelets survive in the circulation between two and seven days,[16] the rapid fall in the platelet count produced by the thrombocytopenic factor must be due to an accelerated loss of platelets from the circulation. There is evidence, however, to indicate that the megakaryocytes of recipients develop qualitative changes within 24 hours similar to those described in idiopathic thrombocytopenic purpura. After approximately three days, the megakaryocytes show an increase in granularity of the cytoplasm, and after five to seven days seem again to be making platelets.[1] These changes are illustrated in figure 3 from bone marrow obtained serially from one recipient. If the thrombocytopenic factor is an antibody, it would be expected that the immunologic properties of platelets and megakaryocytes would be so

16. (*a*) Lawrence, J. S., and Valentine, W. N.: The Blood Platelets: Rate of Their Utilization in the Cat, Blood **2**: 40, 1947. (*b*) Hirsch, E. O., and Gardner, F. H.: The Transfusion of Human Blood Platelets. J. Lab. & Clin. Med. **39**: 556, 1952. (*c*) Hirsch, E. O.; Favre-Gilly, J., and Dameshek, W.: Thrombopathic Thrombocytopenia: Successful Transfusion of Blood Platelets, Blood **5**: 568, 1950.

similar that the antibody would affect both elements. These studies, then, indicate that the thrombocytopenic factor influences both production and destruction of platelets.

The existence of an immunologic thrombocytopenic factor has been suggested by other observations. Evans [17] noted the occasional association of idiopathic acquired hemolytic anemia with thrombocytopenia, and thought that an immunologic mechanism was responsible for both abnormalities. Platelet agglutinins have been detected in the blood of patients who developed thrombocytopenia on the basis of drug idiosyncrasy.[18] Platelets transfused into patients with aplastic anemia survive for four to six days but disappear within several hours from the circulation of patients with idiopathic thrombocytopenic purpura.[19] Lastly, direct proof that antiplatelet antibodies can produce thrombocytopenia has been demonstrated repeatedly in animal experiments.[20] Platelets from the rat, for instance, have been injected into rabbits to produce an antirat platelet serum; when this serum was given to other rats, thrombocytopenia resulted.

This last observation, however, emphasizes the need for caution. It is necessary to determine that the thrombocytopenic factor described above occurred as a causative mechanism in the production of idiopathic thrombocytopenic purpura and did not develop as a result of sensitization to platelets injected into the patients at the time of previous transfusions. The possibility exists that there are different platelet types, just as there are different red cell types. If that is so, then isoimmunization to platelets may result from pregnancy or from transfusions when "incompatible" platelets are involved, in a manner

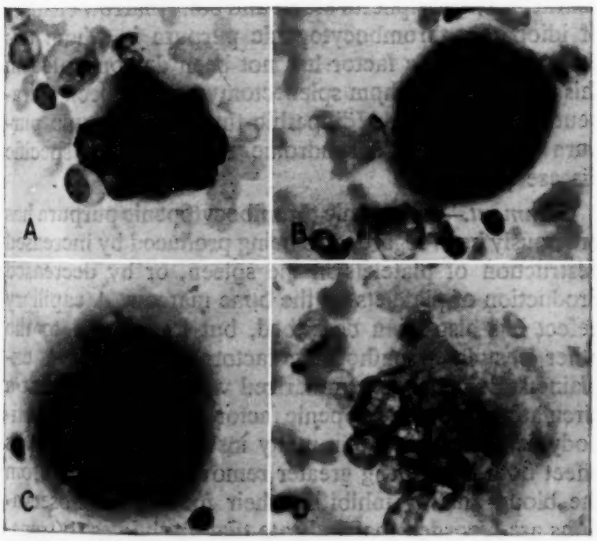

Fig. 3.—Appearance of megakaryocytes in recipient of plasma from a patient with idiopathic thrombocytopenic purpura. *A*, one day after transfusion. *B*, three days after transfusion. *C*, five days after transfusion. *D*, seven days after transfusion.

similar to that for red cells. The following information has already been accumulated to suggest that isoimmunization to platelets does occur in man.

1. The authors have noted on several occasions that when platelet transfusions were given to patients with hypoplastic anemia who previously had received many transfusions, the immediate rise in platelet levels of the recipients was much less than would have been expected if the platelets had survived normally in the circulation.

2. Hirsch and Gardner [16b] have observed that platelets transfused into patients with hypoplastic anemia usually survive, after the first transfusion, for five to seven days. With repeated transfusions, however, there was progressively shorter survival of the transfused platelets, due possibly to the formation of an antibody which was producing rapid destruction.

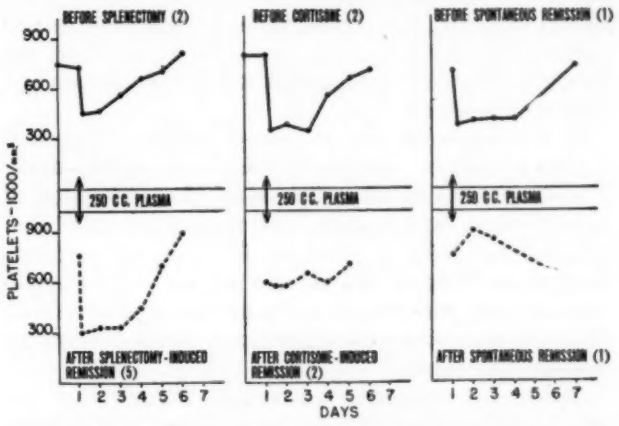

Fig. 4.—The charts at the top indicate the thrombocytopenic effect of plasma from patients with idiopathic thrombocytopenic purpura when transfused into normal recipients. Those at the bottom show results of plasma transfusion after remission was induced by splenectomy or cortisone or occurred spontaneously. In the patients treated by splenectomy, the thrombocytopenic factor persisted, whereas in the cortisone-treated patients and in the patient who had a spontaneous remission, the thrombocytopenic factor could no longer be demonstrated. The figures in parentheses indicate the number of observations.

3. Plasma was obtained from a patient with hypoplastic anemia who had received 547 transfusions. When this was given intravenously in the small amount of only 10 cc. to a patient with chronic myelocytic leukemia and thrombocytosis, it caused a fall in the platelet count of the recipient from 1,670,000 to 620,000 per cubic millimeter. This decrease occurred within one hour, was maximal at two hours, and persisted for several days. No such effect was obtained with normal plasma even in much larger amounts. Plasma was obtained from a second patient with refractory anemia and a leukemoid reaction who had received a few less than 300 transfusions; 250 cc. of this plasma was given intravenously to a normal recipient. There was an immediate fall in the platelet count by the indirect method of Dameshek from 1,052,000 to 580,000 per cubic millimeter and a continued gradual decrease over a period of 48 hours to 141,000 per cubic millimeter. Simultaneous counts done

17. Evans, R. S.; Takahashi, R.; Duane, R. T.; Payne, R. and Liu, Chi-Kong: Primary Thrombocytopenic Purpura and Acquired Hemolytic Anemia, A.M.A. Arch. Int. Med. **87**: 48 (Jan.) 1951.

18. Ackroyd, J. F.: The Cause of Thrombocytopenia in Sedormid Purpura, Clin. Science **8**: 269, 1949.

19. Footnote 2. Hirsch.[16b]

20. Ledingham, J. C. G.: The Experimental Production of Purpura in Animals, Lancet **1**: 1673, 1914. Ledingham, J. C. G. and Bedson, S. P.: Experimental Purpura, ibid. **1**: 311, 1915. Bedson, S. P.: Blood Platelet Anti-Serum, Its Specificity and Role in the Experimental Production of Purpura, J. Path. & Bact. **25**: 94, 1922. Bedson, S. P.: Immunity to Anti-Platelet Serum, J. Path. & Bact. **23**: 176, 1923. Tocantins, L. M.: The Mammalian Blood Platelet in Health and Disease, Medicine **17**: 155, 1938 (No. 2). Elliott, R. H. E. Jr. and Whipple, M. A.: Observations on the Interrelationship of Capillary, Platelet and Splenic Factors in Thrombocytopenic Purpura, J. Lab. & Clin. Med. **26**: 489, 1940. Leonard, M. E., and Falconer, E. H.: Experimental Thrombocytopenia in the Guinea Pig, ibid **26**: 648, 1941. Leonard and Falconer.[16b]

by the direct method of Brecher and Cronkite [21] gave similar results. It should be mentioned that there was also a fall in the white count in each instance; in the patient with chronic myelocytic leukemia there was a decrease from 257,000 to 169,000 per cubic millimeter and in the second recipient from 12,500 to 1,250 per cubic millimeter. This fall was observed immediately following the plasma injection. It is significant that each recipient had a severe reaction with chills, fever, nausea, vomiting and diarrhea; the second patient also had severe dyspnea and developed cyanosis.

4. When plasma from the above patients was added in vitro to platelet suspensions made from normal blood of all four ABO blood groups, marked agglutination of platelets occurred.* Plasma from normal subjects failed to agglutinate these suspensions. Attempts are currently being made to apply this in vitro test for platelet agglutinins to other patients and to the plasma of subjects with idiopathic thrombocytopenic purpura. The results will be reported elsewhere.

Because the evidence indicates so strongly that isoimmunization to platelets probably occurs, it is particularly important that four of the patients with idiopathic thrombocytopenic purpura in whose plasma a thrombocytopenic factor was demonstrated had never been transfused, and had never been pregnant. In these persons isoimmunization to platelets could not have taken place. The presence of a thrombocytopenic factor in these four patients constitutes clear evidence for its importance in the pathogenesis of some cases of idiopathic thrombocytopenic purpura, even though it admittedly is not yet possible in the remaining subjects to rule out isoimmunization as a cause for the factor.

Role of the Spleen.—The good therapeutic response to splenectomy in many patients with idiopathic thrombocytopenic purpura provides proof that the spleen is involved in the pathogenesis of this disease. It has already been noted that some investigators believe that the spleen depresses maturation of megakaryocytes, while others believe that it removes platelets at an accelerated rate. Since the spleen seems to make red cell antibodies in acquired hemolytic anemia,[22] it probably also makes platelet antibodies in those patients with idiopathic thrombocytopenic purpura in whom an immunologic mechanism is of importance. Evidence that the spleen may be involved in destruction of sensitized platelets was obtained by injecting antirat platelet serum into rats whose spleens had been removed and normal litter mates.[23] With large doses, the platelet count fell in both. With smaller amounts, however, there was a platelet decrease in the normal rat, but no significant change in the splenectomized litter mate. This result suggests that high concentrations of thrombocytopenic factor cause destruction of platelets even in the absence of a spleen. When the concentration is smaller, however, the spleen serves an important role in removing platelets from the circulation. Consistent with the above explanation is the fact that the thrombocytopenic factor persists in the plasma of some patients with idiopathic thrombocytopenic purpura, even after a splenectomy-induced remission. The rise in platelets that occurs in such patients would seem to be due to the absence of the splenic removal mechanism, possibly associated with a lower concentration of thrombocytopenic factor. Figure 4 shows the fate of the thrombocytopenic factor in various types of remission. When splenectomy was performed, the factor persisted. Following cortisone-induced remission, there apparently was a reduction in antibody production as might be anticipated. In the case of spontaneous remission, a similar disappearance of antibody occurred.

There remain a significant number of patients with the characteristic peripheral blood and bone marrow changes of idiopathic thrombocytopenic purpura in whom this thrombocytopenic factor has not been demonstrated in this study and in whom splenectomy has not been therapeutically beneficial. Idiopathic thrombocytopenic purpura may well be a syndrome rather than a specific disease entity.

Comment.—Idiopathic thrombocytopenic purpura has previously been regarded as being produced by increased destruction of platelets in the spleen, or by decreased production of platelets by the bone marrow. A capillary defect has also been described, but its relation to the other postulated pathogenic factors has not been explained. Evidence is summarized which indicates that a circulating thrombocytopenic factor, presumably an antibody, is of importance in many instances, and exerts its effect both by causing greater removal of platelets from the blood and by inhibiting their formation. Observations are recorded that indicate that antibodies to transfused platelets may develop. However, this sensitization could not have occurred in four patients with idiopathic thrombocytopenic purpura. Evidence is being presented elsewhere that the spleen is somehow involved in the removal of sensitized platelets. The good therapeutic results obtained with splenectomy may be due to this effect, but the possibility remains that splenectomy may fail to relieve the thrombocytopenia when there is so high a concentration of thrombocytopenic factor that platelet formation remains depressed and destruction accelerated even in the absence of the spleen.

21. Brecher, G., and Cronkite, E. P.: Morphology and Enumeration of Human Blood Platelets, J. Applied Phys. **3**: 365, 1950.

* This in vitro test for platelet agglutinins is performed in the following manner. All surfaces with which the platelets come in contact are made nonwettable by applying a thin coat of silicone ("dri-film" SC-87 [General Electric]) diluted 1 to 10 with petroleum ether, washing immediately 15 to 20 times with distilled water, and drying in an oven. Blood is collected through an 18 gage siliconed needle without a syringe. The first few cubic centimeters of blood are discarded, and then 10 cc. are permitted to flow into a siliconed tube containing 0.3 cc. of a 5% solution of disodium ethylene-diamine tetra-acetate ("sequestrene NA2," supplied by Alrose Chemical Co., Providence, R. I.). The blood is centrifuged for 20 minutes at a centrifugal force of approximately 150 G (1,000 rpm in an International Centrifuge, size SB [manufactured by International Equipment Company, Boston, Mass.]). At this speed, most of the platelets remain in the supernatant plasma; this platelet-rich plasma is transferred to another siliconed tube and placed in the refrigerator until needed. Platelet-free plasma, which is to be tested for agglutinins, is obtained by centrifuging blood collected in a similar manner at 4,000 rpm (2,700 G) for 30 minutes. Then 0.9 cc. of this platelet-free plasma is acidified with 0.1 cc. of the one-third normal citric acid; 0.1 cc. of the platelet suspension is added to 0.1 cc. of the acidified platelet-free plasma in a small siliconed tube. The tube is covered by a strip of "parafilm" (Marathon Corporation, Menasha, Wis.) and placed in a 37 C waterbath for one hour, and then put into the refrigerator for two additional hours. It is then removed, centrifuged at 150 G for two minutes, shaken 15 to 20 times by hand, poured onto a siliconed, welled slide, and examined microscopically for agglutination.

22. Wagley, P. F., Shen, S. C., Gardner, F. H., and Castle, W. B.: The Spleen as a Source of a Substance Causing Agglutination of the Red Blood Cells of Certain Patients with Acquired Hemolytic Jaundice by an Antihuman Serum Rabbit Serum (Coomb's Serum). J. Lab. & Clin. Med. **33**: 1197, 1948.

23. Harrington, W. J., Sprague, C. C., and Moore, C. V.: Immunologic Aspects of Idiopathic Thrombocytopenic Purpura, Ann. Int. Med., to be published.

The thrombocytopenic factor, however, has not been demonstrated in the blood of most children with idiopathic thrombocytopenic purpura, and has not been found in all adult patients. The disease, therefore, may be caused by a variety of factors, an immunologic mechanism being only one.

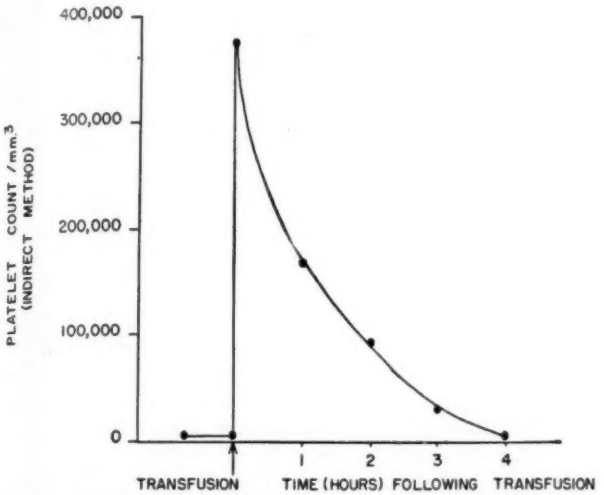

Fig. 5.—Survival of platelets from 586 cc. of whole blood transfused into a patient with idiopathic thrombocytopenic purpura who had a high titer of platelet agglutinins.

EXPERIENCES WITH PLATELET TRANSFUSIONS

Stimulated by the fact that the formed elements of blood are currently being discarded as large amounts of plasma are again being collected under the national blood program, several groups of investigators are exploring the possibility of salvaging these cells. One facet of this problem is to determine whether platelet transfusions would be therapeutically valuable if the platelets could be saved. The results already reported and those to be summarized here indicate, unfortunately, that platelet transfusions would probably have only a very limited usefulness even if technical difficulties were solved.

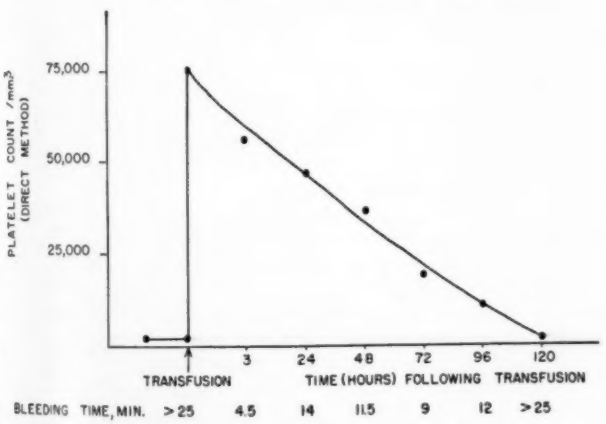

Fig. 6.—Survival of platelets from 600 cc. of whole blood transfused into a patient with aplastic anemia.

Several different transfusion techniques have been used. Blood has been drawn from polycythemic donors into siliconed syringes and given directly without use of anticoagulants to thrombocytopenic recipients.[2] Originally, collection was performed using plastic bags containing ACD solution, the platelets concentrated by centrifugation, and injected in the form of concentrated suspensions. More recently, disodium ethylene-diamine tetra-acetate ("sequestrene" NA2) has been substituted for ACD solution, with rapid cooling of the blood during collection.[24] The authors have employed the following method. Polycythemic patients with thrombocytosis were used as donors whenever possible. Siliconed bottles, plastic tubing and needles coated with either "drifilm" (General Electric) or "arquad 2C" (Armour and Company), were used in order to make all surfaces nonwettable so that loss of platelets would be minimal. The anticoagulant solution in the bottle has been either 20 cc. of a 4.5% (isotonic) solution of disodium ethylene-diamine tetra-acetate or 750 mg. of the same material in 100 cc. of 0.7% sodium chloride solution. The blood was chilled as it was collected and transfused as soon as possible. In one instance the blood was kept for 24 hours; the duration of survival of the transfused platelets in the recipient was five days.

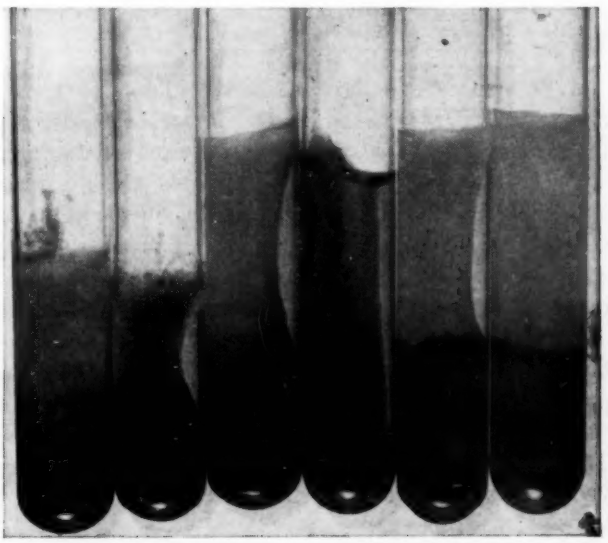

Fig. 7.—Altered clot retraction in patient with aplastic anemia following platelet transfusion. First sample on left was drawn immediately prior to transfusion, the second sample immediately following transfusion and the next four samples were drawn at 24-hour intervals thereafter.

When platelets were transfused into patients with idiopathic thrombocytopenic purpura, the immediate post-transfusion recovery in the circulation of the recipient was usually very good, but the platelets disappeared within a few hours. This result is similar to that obtained by other workers,[19] and has already been cited as evidence indicating the existence of a thrombocytopenic factor in idiopathic thrombocytopenic purpura. The short survival time of transfused platelets in a patient known to have the thrombocytopenic factor in her blood is illustrated in figure 5. The disappearance rate was somewhat slower in those patients in whom no antiplatelet factor could be demonstrated. In spite of the short survival time, however, the hemorrhagic manifestations and the prolonged bleeding time were occasionally reversed for brief periods, as others have already indicated.[19] This effect was so transient, however, that it

24. Dillard, G. H. L., Brecher, G., Cronkite, E. P.: Separation, Concentration and Transfusion of Platelets, Proc. Soc. Exp. Biol. & Med. 78: 796, 1951.

would not be a satisfactory form of medical management for patients with idiopathic thrombocytopenic purpura; it might occasionally be beneficial while preparations are being made for splenectomy.

Five platelet transfusions given to three subjects with aplastic anemia showed survival times of four to six days. A representative result is charted in figure 6. The effect of the transfused platelets in increasing clot retraction is illustrated in figure 7. Hirsch and Gardner have reported a similar experience.[16b] These results are good enough to be of practical value in helping to support a patient during periods of temporary depression of platelet formation. They are limited, however, by the fact that platelet antibodies seem to develop, so that with repeated transfusions the platelet survival becomes progressively shorter.[16b] If platelet types could be determined in a practical manner, so that platelets of the same serologic type could be given, the therapeutic value of these transfusions might be greatly increased.

CONCLUSIONS

1. The plasma of some patients with idiopathic thrombocytopenic purpura contains a thrombocytopenic factor that lowers the level of circulating platelets and damages megakaryocytes. 2. The spleen probably plays at least a dual role in this disease, particularly in the removal of sensitized platelets and sharing in antibody production. 3. Specific platelet groups probably exist; isoimmunization by incompatible platelet transfusions seems to occur. 4. Platelet transfusions are of limited therapeutic importance but may be of value in idiopathic thrombocytopenic purpura immediately prior to splenectomy and in acute aplastic anemias until the bone marrow recovers. Their effectiveness is limited by the fact that platelet survival tends to decrease progressively when repeated transfusions are given.

600 S. Kingshighway Blvd. (Dr. Sprague).

Intrinsic Asthma.—We have gotten away from the old idea that the paranasal sinuses were important foci of infection in relation to asthma. While at times this may be true, the sinusitis, especially the hyperplastic form, more often is a result of the allergic processes rather than its cause. Radical operations should not be done unless there exists extensive suppuration which cannot be improved by other methods, especially modern biotherapy. We seldom have had to resort to such procedures in our patients and, as I have reported elsewhere, the assumption that asthma is of infectious or intrinsic origin often is based upon the inability to find the specific cause; it then becomes a simple matter to conclude that the patient has a bacterial allergy and to treat him accordingly. While the asthma may be due to bacterial allergy, such a conclusion should not be reached until every effort has been made to find a nonbacterial factor or, if not, to treat the patient as though it were nonbacterial. Wherever necessary, of course, vaccines, whether stock or autogenous (especially those obtained by bronchoscopic aspiration), may be useful adjuncts provided they are used with caution and in small doses. In the past three or four years, we have been employing the intracutaneous method of administration for vaccines and have found the tendency to general reactions greatly lessened. —Louis Tuft, M.D., Allergy Problems in General Practice and Their Management, *American Practitioner and Digest of Treatment*, September, 1952.

CLINICAL NOTES

OBSTRUCTION OF THE SUPERIOR VENA CAVA OF TWENTY-FIVE YEARS' DURATION

Leonard B. Rose, M.D., Albany, N. Y.

The survival period following obstruction of the superior vena cava depends to some extent on the underlying cause of the obstruction—a benign lesion of gradual onset would be expected to result in the longest survival. While obstruction of the superior vena cava due to tumor or aneurysm is not uncommon, accounting for 70% to 85% of the cases, benign lesions causing obstruction of this vessel, such as mediastinitis and thrombophlebitis, are relatively uncommon.[1] The present case is reported because of the following points of interest: (1) gradual onset of signs and symptoms during and after a period of recurrent severe infections of the chest wall, strongly suggesting thrombophlebitis as the cause, (2) involvement of the azygos vein, as proved by angiograms and clinical tests (described elsewhere [2]), (3) prolonged survival period of 25 years, indicating adequate compensatory collateral circulation, and (4) minimal symptoms after 25 years, the diagnosis having been made incidental to hospitalization necessitated by symptoms thought to be not directly related to the obstruction of the superior vena cava.

REPORT OF A CASE

First Admission.—A 57-year-old white man was admitted to the medical service of the Albany Veterans Administration Hospital on Sept. 13, 1951, because of recurrent bleeding from the nose and progressive shortness of breath.

Three and one-half months before entry the patient began to have frequent epistaxes, which recurred in spite of vigorous treatment, including two admissions to a private hospital. The last episode ended a week before admission. No history suggestive of hemorrhagic tendency was elicited. He had a perforated nasal septum as a result of surgery many years previously. For three years prior to admission he had experienced progressive shortness of breath on exertion; one flight of stairs now produced dyspnea and fatigue. During the past several years chronic cough gradually developed, especially in the morning, productive of small to moderate amounts of pearl gray and greenish phlegm. There had never been any hemoptysis. There was no history of chest pain, palpitation, or edema.

In 1927 he noted the gradual appearance of distended tortuous veins over the anterior part of the chest and at that time first began to complain of dizziness, especially on arising and bending over. His face became puffy, with a bluish hue, which became worse when he reclined, bent forward, or after a shower. His collar size increased, although he had not gained any weight. There had been no distinct acute episode, but he recalled clearly that from 1918 until 1929 he had had multiple severe furuncles and carbuncles on the trunk and in both axillas, which had continued to trouble him less frequently and less severely until the present. Because of his complaints of dizziness and some brief syncopal episodes, he was hospitalized for three weeks at the Brooklyn Jewish Hospital in 1929 and later treated by Dr. Mil-

From the Medical Service of the Veterans Administration Hospital and the Albany Medical College, Albany, N. Y.

1. McIntire, F. T., and Sykes, E. M., Jr.: Obstruction of the Superior Vena Cava: Review of Literature and Report of 2 Personal Cases, Ann. Int. Med. **30**: 925-960 (May) 1949.

2. Hussey, H. H.; Katz, S., and Yater, W. M.: Superior Vena Caval Syndrome: Report of 35 Cases, Am. Heart J. **31**: 1-26 (Jan.) 1946.

ton G. Wasch of Brooklyn. In a recent communication Dr. Wasch stated that a broadened nonpulsating superior mediastinal shadow was found in 1929 but that unfortunately the original roentgenograms were no longer available. At that time there was evidence of venous obstruction. Biopsy was not attempted. X-ray treatments were given in 1929 and again sporadically in 1930 and 1931, because Dr. Wasch strongly considered the diagnosis of lymphoblastoma although the patient's subsequent course made him entertain the possibility of thrombosis. The patient stated that after the x-ray treatment the cyanosis gradually became less, the dizziness became less troublesome, and there were no further syncopal episodes. The past history was otherwise not contributory. He had not worked in several years, principally because of emotional difficulties and more recently because of the cough and dyspnea.

Physical examination on admission disclosed a tall, thin, plethoric-looking, somewhat cyanotic white man who coughed frequently. The rectal temperature was 99 F (37.2 C), pulse rate 72, respirations 20, blood pressure 130/70 mm. Hg, weight 157 lb. (71.2 kg.), and height 73 in. (185.4 cm.). The face and neck showed a cyanotic and somewhat reddish hue; when the patient lay supine, the cyanosis deepened and a line of demarcation appeared at the level of the clavicles (so-called Stokes' collar). The eyes were prominent and the eyelids slightly edematous. The pupils were equal and active and the retinal veins full and tortuous. Both ear drums contained large perforations. There was a large defect in the nasal septum. The tongue was slightly coated, and small varicosities were present along its lateral margins. The oral mucosa showed a slight bluish tinge, and the pharynx appeared to be a little congested.

There were numerous prominent tortuous superficial veins in the neck. There were many dilated tortuous superficial veins over the chest wall anteriorly that crossed the costal margins and continued down over the abdomen to the pubis. Markedly tortuous veins were present in both axillas and distended veins were prominent in both antecubital fossae and along both arms (fig. 1). A 10-cm. square hyperkeratotic patch with multiple telangiectases was present in the interscapular area. The entire trunk was covered with a cystic and pustular acneiform eruption interspersed with old healed scars of previous lesions.

The chest was symmetrical with an increased anteroposterior diameter. Expansion was only fair. The percussion note was hyperresonant, and there was slight diminution of breath sounds and prolongation of the expiratory phase of respiration over

Fig. 1.—Infra-red photograph showing collateral venous circulation of the anterior chest wall.

both lower lobes. The heart was not enlarged, nor was there any increased retromanubrial dulness. The tones were distant, and no murmurs were heard. Examination of the abdomen, rectum, and genitalia disclosed no abnormalities. The upper extremities shared the cyanotic hue of the head and neck, while the lower extremities, in contrast, were of normal color. There was no edema found in the lower extremities. The radial, dorsalis pedis, and posterior tibial pulsations were of good and equal volume. No significant lymphadenopathy was found. The results of the neurological examination were normal.

Laboratory Data: Results of routine urinalysis, blood cell count, and serologic tests were within normal limits. Results of hemostatic tests and sputum examinations were unremarkable.

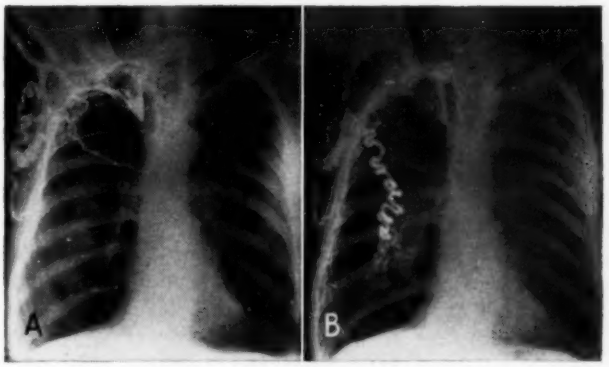

Fig. 2.—*A*, phlebogram taken three seconds after the injection of iodopyracet in right arm vein. Note the abnormal complex of veins in the right upper mediastinum as well as complete obstruction at the point where the innominate vein begins. *B*, phlebogram taken six seconds after the injection. Note the huge internal mammary veins ending in tortuous superficial epigastric veins seen within the cardiac shadow.

X-ray Studies: The admission roentgenogram of the chest showed an emphysematous contour of the thoracic cage, obliteration of the left costophrenic angle, and considerable increase in the linear markings of both lung fields. Fluoroscopy of the chest revealed an increased density along the right upper mediastinum, prominent pulmonary vessels, flattening of the diaphragms, and limited respiratory movements. Special roentgenograms taken after fluoroscopy demonstrated a density along the right upper mediastinum, no deformity of the bronchial tree, and a group of heavily calcified nodes lying against the right side of the trachea at the bifurcation of the main stem bronchi.

Special Studies: A phlebogram performed by the rapid injection of 50 cc. of 70% iodopyracet into the right median basilic vein with roentgenograms taken at three and six seconds showed that the widening of the upper mediastinum was composed mainly of abnormal veins (fig. 2). The right subclavian vein appeared to be constricted and accompanied by numerous collateral channels. Complete obstruction was present just beyond the beginning of the innominate vein. No dye entered the heart during the time of exposure, but all was deviated through tremendously dilated and tortuous collateral veins over the upper part of the thorax. The iodopyracet was seen to enter a huge internal mammary vein on the right, which descended and joined with the huge superficial dilated veins over the abdomen.

Venous pressures in all four extremities were as follows: right median basilic, 380 mm. (of citrate solution); left median basilic, 340 mm. (average normal for these veins, 110 mm.); left greater saphenous, 100 mm.; and right greater saphenous, 140 mm. (average normal for these veins, 125 mm.). A paradoxical effect of respiration on the venous pressure in the upper extremities was noted.

Hospital Course: No epistaxis occurred throughout the hospital stay. The chronic bronchitis and emphysema were treated with bronchodilators, antibiotics, and special respiratory exercises. The cough improved, and the exertional dyspnea diminished. The dermatologist, who considered that the hyperkeratotic area on the back was a roentgen dermatitis, prescribed an emollient for this as well as local treatment for the acne, with good results. The patient was discharged on Dec. 1, 1951, with instructions to continue the special respiratory exercises.

Second Admission.—The patient was readmitted on Feb. 4, 1952, for follow-up studies and completion of dental treatment. He had continued the respiratory exercises at home. The improvement in the cough, dyspnea, and exercise tolerance had continued, and he felt well. On cold mornings, when walking out briskly to buy his newspaper, he noted a pressure anteriorly

in the chest, but this was relieved by slowing down or stopping. Otherwise, he was more comfortable than before his first admission. Results of physical examination, routine laboratory studies, chest roentgenogram, and an electrocardiogram were not significantly different from those of the first admission. The vital capacity was 3.3 liters and the three-second vital capacity 2.2 liters. The pressure in the left median basilic vein was 280 mm., which rose on constriction of the chest wall with a band and also rose 20 mm. on exercising the left hand for one minute. His dental work was completed, and he was returned to the care of his private physician on Feb. 8.

COMMENT

The literature on obstruction of the superior vena cava has been reviewed extensively elsewhere.[1] Because of the prolonged survival period in this case and in spite of the earlier roentgen therapy, a benign cause must be considered. The fact and site of the occlusion have been demonstrated by the clinical studies and the phlebograms. The history of severe carbuncles and furuncles of the chest wall for several years before the appearance of evidence of collateral circulation strongly suggests thrombophlebitis with propagation of the thrombus as the cause. The presence of heavily calcified nodes along the right tracheal border further suggests the possibility of an old chronic mediastinitis, which may well have accompanied the thrombophlebitis. Thus, the combination of mediastinal lymphadenitis and thrombophlebitis resulting in occlusion of the superior vena cava would be a reasonable explanation of the pathogenesis. It is of passing interest that the incidence of mediastinitis of all types is declining and the number of cases of superior vena caval obstruction due to benign causes may be diminishing as well.[1]

Prolonged survival has been reported in rare instances. McCord, Edlin, and Block described a patient who died 50 years after the development of evidence of collateral circulation after a febrile illness in childhood, the superior vena cava having been completely obstructed by a fibrocalcific mass.[3] Glushien and Mansuy have described a patient living and working 36 years after a rather sudden onset of superior vena cava obstruction.[4] In that case, although the superficial dilated tortuous veins continued down over the abdomen, the azygos vein was considered not to be occluded because the venous pressure in the arms did not rise when a constricting band was applied to the chest wall and because the venous pressure fluctuated normally with respiration. The authors concluded that, despite the functioning of the azygos vein as a superior vena cava, some blood from the upper part of the body was being returned via the inferior vena cava. Renbourn reported a case in which the collaterals had been present for more than 50 years without subjective symptoms.[5] However, in the case presented here, the presence of large collateral vessels descending over the abdomen to the pubis,[6] the paradoxical effect of respiration on the venous pressure,[7] the rise in venous pressure with constriction of the veins crossing the costal margin,[7] and the phlebograms are considered evidence favoring the inclusion of the azygos vein in the obstruction. The prolonged survival period is considered even more remarkable because the blood from the upper regions of the body had to be returned via the inferior vena cava.

Hussey, Katz, and Yater, in their series [2] listed the symptoms and signs of the superior vena caval syndrome (dilated veins, edema, dyspnea, cough, pleural effusion, cyanosis, hoarseness, dysphagia, drowsiness, convulsions, and facial pain) and attempted to delineate those thought to be due to the venous obstruction per se from those brought about by the causative factor. In the case herein reported, the patient sought hospitalization for disabilities thought to be due in only a small measure to the long-standing venous obstruction. At the time of admission the symptoms arising from the obstruction were relatively mild, although the signs—facial edema, cyanosis, distended tortuous veins, and increased venous pressure in the upper extremities—were present. The recent progressive dyspnea and cough were considered to be due to pulmonary emphysema resulting from chronic bronchitis, pulmonary fibrosis, and degenerative factors. The epistaxis was never explained satisfactorily.

SUMMARY

A case of obstruction of the superior vena cava including the orifice of the azygos vein, probably due to thrombophlebitis and mediastinal lymphadenitis caused by multiple severe skin infections of the trunk, is reported. The patient, at the time of writing, had survived 25 years and, in spite of the classical signs, experienced only minimal symptoms from the venous obstruction.

3. McCord, M. C.; Edlin, P., and Block, M.: Superior Vena Caval System Obstruction, Dis. Chest **19**: 19-27 (Jan.) 1951.

4. Glushien, A. S., and Mansuy, M. M.: Superior Vena Caval Obstruction with Survival After 36 Years, Angiology **2**: 210-216 (June) 1951.

5. Renbourn, E. T.: Thrombosis of Superior Vena Cava, Thorax **1**: 257-262 (Dec.) 1946.

6. Hinshaw, H. C., and Rutledge, D. I.: Lesions in Superior Mediastinum Which Interfere with Venous Circulation, J. Lab. & Clin. Med. **27**: 908-916 (April) 1942.

7. Hitzig, W. M.: On Mechanisms of Inspiratory Filling of the Cervical Veins and Pulsus Paradoxus in Venous Hypertension, J. Mt. Sinai Hosp. **8**: 625-644 (Jan.-Feb.) 1942.

ROENTGENOGRAPHIC LOCALIZATION OF DESCENDING AORTA

USE IN INFANT WITH TETRALOGY OF FALLOT

Harry F. Zinsser Jr., M.D.
Truman G. Schnabel Jr., M.D.
and
Julian Johnson, M.D., Philadelphia

The shunting procedures devised by Blalock [1] and Potts [2] are accepted techniques for the treatment of certain children with congenital heart disease characterized by inadequate blood supply to the lungs. In managing cyanotic children it is customary, if possible, to delay surgery until they are between 4 and 8 years old. At that time special studies, including angiocardiography, may be done, if necessary, to determine the nature of the intracardiac lesion as well as the size and position of the pul-

This work was done during the tenure of a research fellowship of the American Heart Association held by Truman G. Schnabel Jr.

From the Edward B. Robinette Foundation of the Medical Clinic, Hospital of the University of Pennsylvania and the Department of Surgery, School of Medicine, University of Pennsylvania.

1. Blalock, A., and Taussig, H. B.: The Surgical Treatment of Malformations of the Heart in Which There is Pulmonary Stenosis or Pulmonary Atresia, J. A. M. A. **128**: 189 (May 19) 1945.

2. Potts, W. J.; Smith, S., and Gibson, S.: Anastomosis of the Aorta to a Pulmonary Artery: Certain Types in Congenital Heart Disease, J. A. M. A. **132**: 627 (Nov. 16) 1946.

monary artery and aorta. Occasionally, an infant is so severely handicapped that surgical intervention becomes imperative before the optimal age is reached. It is our experience that the Potts-Smith-Gibson operation, which produces a direct communication between the descending aorta and the pulmonary artery, is technically most

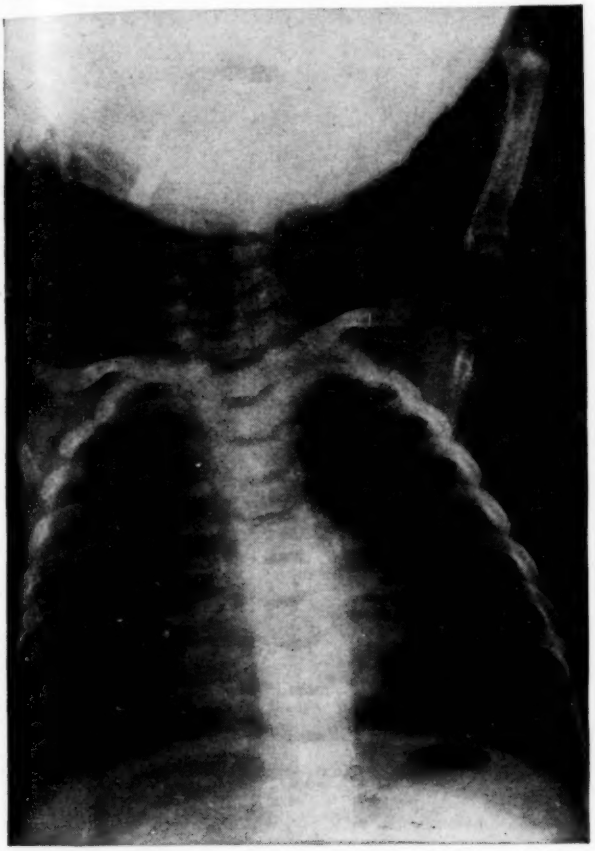

Fig. 1.—Posteroanterior roentgenogram, interpreted as representing dextrocardia and right aortic arch. Note the extremely clear and avascular lung fields.

suitable for infants. Utilization of this procedure demands a prior knowledge of the location of the descending aorta, since its position determines the side of the operative approach. The use of barium orally to outline the esophagus, or an over-penetrated Bucky film delineating the trachea [3] can furnish indirect evidence of the location of the aortic arch, but these methods do not unmistakably locate the descending aorta. Angiocardiography, on the other hand, can clearly define the course of the aorta; however, infants who require constant oxygen administration react poorly to most diagnostic procedures, and angiocardiography has its greatest mortality rate in this group of patients. The ideal procedure would be one that would, with simplicity and minimal risk, ascertain the location of the descending aorta. In the case reported below, such a method was devised by the technique of inserting a small polyvinyl catheter into the aorta through a no. 21 gage needle placed in the femoral artery.

REPORT OF A CASE

The patient, a 4½-month-old boy, was markedly cyanotic. He was the fourth child of a 36-year-old woman who, in the sixth month of pregnancy, went into a coma from previously unrecognized diabetes. During labor she again became comatose and had a convulsion. The child was born on May 26, 1951, by breech presentation after 15 hours of labor; he weighed 8 lb. 6 oz. (3,799 gm.). Cyanosis was present at birth, and oxygen was administered during the first 12 days of life. He ran a temperature as high as 105 F during the neonatal period and had hyperinsulinism, which required treatment with glucose. He was kept at home until Oct. 11, 1951, at which time he had a "spell," with increased cyanosis and extremely labored respirations, necessitating oxygen therapy at another hospital. He was transferred to the Hospital of the University of Pennsylvania on Oct. 15, 1951.

On admission, the patient's temperature was 98 F, pulse 120, and respirations 36 per minute. His weight was 13 lb. 9 oz. (6,152 gm.), and he was 60 cm. long. He was markedly cyanotic. The lungs were clear. The heart sounds were heard well centrally and far to the right. A systolic murmur was present on both sides of the sternum; it was most intense to the left, just below the pulmonary area, where a slight thrill was felt. The liver was palpable 3 cm. below the right costal margin, and tympany was elicited in the left upper quadrant.

The chest roentgenogram (fig. 1) was interpreted as showing dextrocardia and a right aortic arch; however, on fluoroscopy, in the oblique positions, the apex was seen to point forward, and the appearance was not that of a true dextrocardia. The

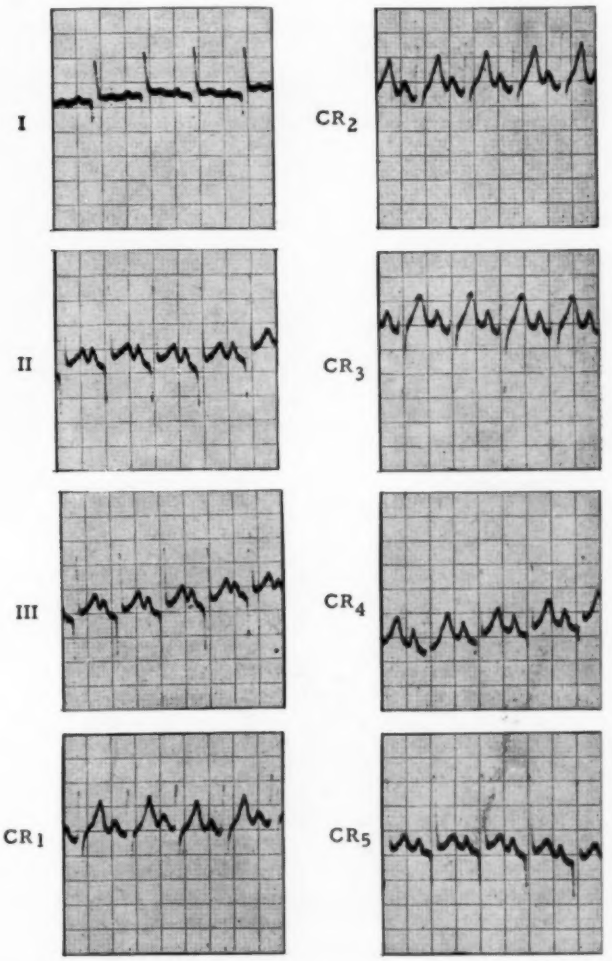

Fig. 2.—Electrocardiogram showing bizarre QRS complexes. Note upright P wave in lead 1, which was against a diagnosis of complete dextrocardia.

lung fields were extremely clear, suggesting an inadequate blood supply. The electrocardiogram (fig. 2) was abnormal but did not show complete dextrocardia. The blood count on admission showed a hemoglobin of 15.8 gm. (Klett tube and photoelectric

3. Ash, R.: Position of Aortic Arch and Descending Aorta: Radiologic Signs in Childhood, Am. J. Roentgenol., to be published.

colorimeter method), a red blood count of 6.6 million, and a hematocrit of 62%.

From the time of admission the patient grew steadily worse. Any attempt to maintain him out of oxygen resulted in marked respiratory difficulty and increasing cyanosis. On Oct. 24, 1951, the hemoglobin was reported to be 17.6 gm. and the red blood count 6.8 million. Digitalization was begun because the liver was increasing in size.

Although the diagnosis was not proved, it seemed most likely that a tetralogy of Fallot was present and that immediate surgery was necessary to prevent death. The child's condition was too critical to permit angiocardiography, which would have ordinarily been employed to define the anatomic defects. It was thought that esophageal contrast techniques might fail to provide the exact knowledge of the course of the descending aorta, which is essential to the successful completion of the Potts-Smith-Gibson anastomosis. At best, surgery entailed an extreme risk, and one could ill afford to enter the wrong side of the chest.

Small polyvinyl catheters introduced through no. 21 gage needles have been used extensively for intra-arterial pressure measurements.[4] These catheters (fig. 3) are not in themselves radiopaque, but it was thought that they could be used to delineate the aorta if some contrast material could be forced into the very small lumen. By this method it is not possible to inject enough material to opacify the aorta but simply to outline the course of the catheter itself. On Oct. 26, 1951, a small catheter was inserted through a no. 21 gage needle that had been placed into the exposed femoral artery. The opacified catheter was advanced from the femoral artery into the aorta and showed the descending aorta to the left of the spine (fig. 4). In this instance efforts to enter the artery through the skin failed, but a percutaneous technique might be successful in other patients.

Immediately following catheterization, a left thoracotomy was performed. A small pulmonary artery was located, and a direct aortopulmonary anastomosis 7 mm. in length was made. The procedure was well tolerated and resulted in a prompt improvement in the patient's color.

The postoperative period was essentially uneventful. The baby's color remained pink, and he required no oxygen therapy. He was able to take nourishment in normal fashion for the first time since admission and gained weight steadily until his discharge on Nov. 8, 1951.

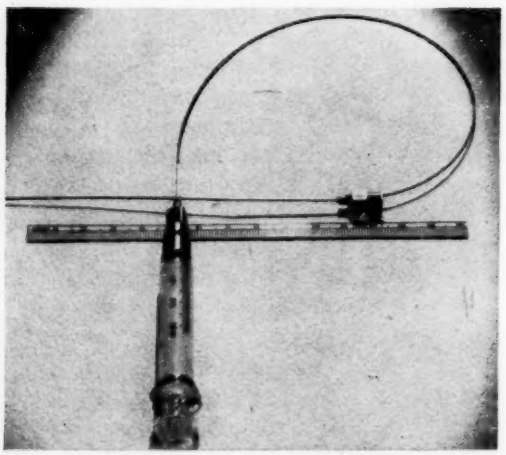

Fig. 3.—Small polyvinyl catheter passing through a special no. 21 gage needle. The opaque material was injected by syringe through a no. 26 gage hypodermic needle into the catheter.

SUMMARY AND CONCLUSIONS

1. In cyanotic patients with congenital heart disease, shunting operations cannot always be postponed until the optimal age of 4 to 8 years is reached.

2. When operation becomes imperative in the cyanotic infant, it is our experience that the Potts-Smith-Gibson operation is technically most suitable.

3. A successful anastomosis of this type requires a knowledge of the location of the descending aorta.

4. The usual methods for locating the aorta are often either uncertain or unsafe for seriously ill infants.

5. The use of a small polyvinyl catheter to delineate the aorta is a simple and reliable procedure.

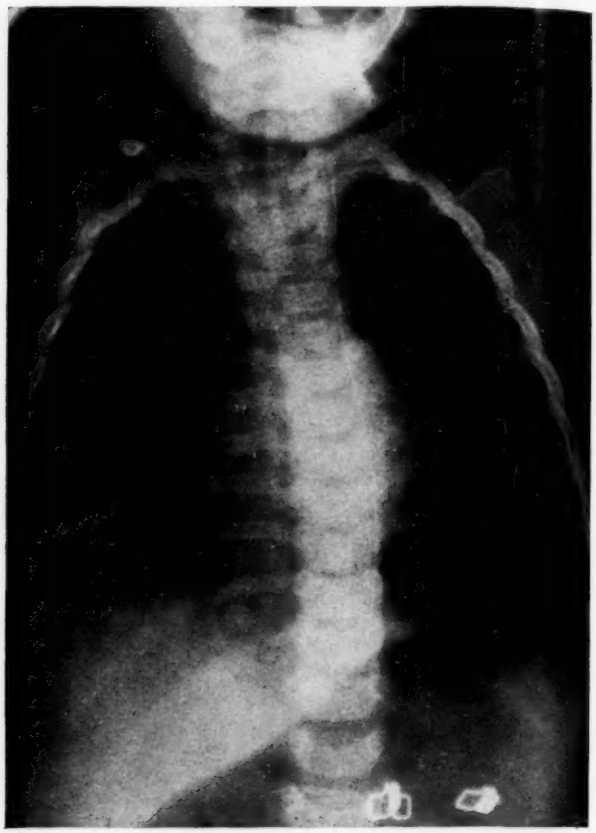

Fig. 4.—Opacified polyvinyl catheter lying in the descending aorta to the left side of the spine and passing up into the left common carotid artery.

6. A case of tetralogy of Fallot in a 5-month-old infant is reported to illustrate the above-mentioned points.

36th & Spruce Sts.

4. Schnabel, T. G., Jr., and others: A Technic of Vascular Catheterization with Small Plastic Catheters. Its Utilization to Measure the Arterial Pulse Wave Velocity in Man, Circulation 5: 257, 1952.

First Papers on Isolation of Insulin.—Banting and I presented our work to the Medical Faculty at a departmental seminar in the autumn of 1921, and our findings were later published in two papers under our names in the *Journal of Laboratory and Clinical Medicine*. These papers give the first detailed account of our isolation of insulin. We were given the impression that a member's name was necessary for the acceptance of a paper to be read at the meeting of the American Physiological Society, and for this reason Professor Macleod's was added to the preliminary paper presented in December, 1921. Banting and I always hoped that our article on "The Internal Secretion of the Pancreas," which appeared in the February, 1922, issue of the *Journal of Laboratory and Clinical Medicine* and which we wrote for and presented to our Medical Faculty on Nov. 14, 1921, would be universally accepted for what it in fact was, the original record of our work. The paper which bore, in addition, the name of the Head of the Department was a summary of the longer one. We prepared it later, but it appeared in print first.—Best, Charles H., Insulin: The Banting Memorial Lecture 1952, *Diabetes*, July-August, 1952.

REPAIR OF FUNNEL CHEST USING SUBSTERNAL OSTEOPERIOSTEAL RIB GRAFT STRUT

REPORT OF A CASE WITH FOUR YEAR FOLLOW-UP

James E. Dailey, M.D., Houston, Texas

An excellent and thorough review of the literature dealing with funnel chest deformity was made in 1938 by Alton Ochsner and Michael DeBakey.[1] They described 32 operative techniques used since 1911 to correct this deformity, commonly known as pectus excavatum. These operations were divided into three types. The first type consisted of procedures involving varying degrees of chondrosternal resection, by which the structural defect was removed but the physiology of respiration was also disturbed. In the second type T-sternotomy procedures were explored, with or without costal cartilage division plus external traction. This method was extensive and complicated, and the condition was likely to recur. The third type involved sternal mobilization and costochondral division or resection, also with external sternal traction. This method was mentioned as the best.

The only other treatment used in the past was conservative or nonsurgical, and consisted of breathing and postural exercises, application of various orthopedic appliances, and use of an adhesive or suction traction apparatus. These measures were entirely unsuccessful. In brief, the multiplicity of the aforementioned precedures suggested the true state of affairs, namely, that the ideal treatment or operative technique had not yet been found.

The reasons why these patients should be operated on can be found in an article by A. Lincoln Brown and Orrin Cook,[2] who described three groups of symptoms: (1) cardiac symptoms such as tachycardia, arrhythmia, substernal distress and dyspnea as manifested late in the course of the disease; (2) respiratory symptoms, which predominate in all age groups; and (3) psychological complaints, which are most noted in the second decade. Many other authors, such as Conrad Lam and Roy D. McClure,[3] Charles W. Lester,[4] Ralph Dorner, Philip G. Keil, and Donald J. Schissel,[5] have reported instances of cardiac embarrassment caused by this condition owing to displacement of the heart on its axis even to the point of cardiac failure.

The age of the patient influences the type of operative procedure to be employed. A simple operation proposed by A. Lincoln Brown [6] in 1939, consisting of sectioning the substernal attachments of the diaphragm, seems to be the one best suited for children up to 18 to 24 months old before the sternum becomes fixed in the retracted position. After this age, however, some type of major procedure must be used.

The results of the previously mentioned major procedures were far from satisfactory. Recurrences were many, and the external traction apparatus, casts, and splints were cumbersome. It is the purpose of this article to describe a new technique for repair of funnel chest deformity. This method consists of removal of the deformed cartilages, elevation of the sternum, and holding it in position by means of an osteoperiosteal rib graft placed beneath the sternum as a strut. This technique is to be used in adults or persons who have attained major growth and fixation of the bone.

This operation was devised and performed for the first time on a 13-year-old girl on Feb. 27, 1948 (fig. 1). It was first proposed in my discussion of C. W. Lester's [4] article on funnel chest in 1949 and again in discussion of a similar paper by R. A. Dorner and co-workers [5] in 1950. Since then Herbert D. Adams [7] has described valuable modifications of this technique in "Surgical Practices of the Lahey Clinic, 1951."

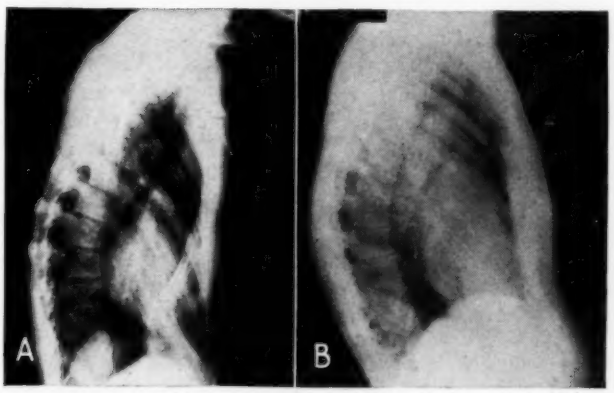

Fig. 1.—*A*, lateral roentgenogram showing the relation of the sternum to the spine preoperatively. *B*, a lateral roentgenogram made two years postoperatively.

TECHNIQUE

The patient was placed in the left lateral position, and an incision was made over the ninth rib on the right chest. The muscles were divided, and the rib was exposed. The periosteum was then incised along the upper and lower borders of the rib, and about 7 in. (17.8 cm.) was resected subperiosteally, leaving the outer covering of periosteum attached to the rib segment. The anterior portion of this particular rib was selected because it was rather broad and flat and had only a slight curve. The segment of rib was then placed in saline solution to keep it moist. The wound was closed in layers.

The patient was then placed on her back, and an inverted "Y" shaped incision was made over the anterior portion of the body of the sternum to the xyphoid. The incision then followed the costal margins for about 2½ in. (6 cm.) on each side. A single straight longitudinal incision, however, would suffice. The flap on each side was dissected back, exposing the entire sternum, cartilages, and ribs. The sternum was flat, and the deformity consisted of acute anterior angulation of the cartilages from the third to and including the seventh rib. The xyphoid process projected forward at a right angle to the body of the sternum. The perichondrium was incised and reflected, and the cartilages from the third to the seventh rib on each side were cut. These,

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1. Ochsner, A., and DeBakey, M.: Chone-Chondrosternon: Report of a Case and Review of the Literature, J Thoracic Surg. **8**: 469, 1939.

2. Brown, A. L., and Cook, O.: Cardio-Respiratory Studies in Pre and Postoperative Funnel Chest (Pectus Excavatum), Dis. Chest **20**: 378, 1951.

3. Lam, C. R., and McClure, R. D.: Decompression of the Heart in Severe Scoliosis: Report of a Case, J. Thoracic Surg. **12**: 517, 1943.

4. Lester, C. W.: Funnel Chest and Allied Deformities of the Thoracic Cage, J. Thoracic Surg. **19**: 507, 1950.

5. Dorner, R. A.; Keil, P. G., and Schissel, D. J.: Pectus Excavatum: Case Report with Pre- and Postoperative Angiocardiographic Studies, J. Thoracic Surg. **20**: 444, 1950.

6. Brown, A. L.: Pectus Excavatum (Funnel Chest) Anatomic Basis: Surgical Treatment of Incipient Stage in Infancy: and Correction of Deformity in Fully Developed Stage, J. Thoracic Surg. **9**: 164, 1939.

7. Adams, H. D.: Costosternoplasty with Rib Strut Support for Funnel Chest in Adults, in Surgical Practice of the Lahey Clinic, Philadelphia, W. B. Saunders Company, 1951.

along with the sternum, were lifted upwards, with careful dissection of the pleura and the mediastinal structures beneath. The cartilages were trimmed off close to the sternum, and the xyphoid process was removed. The lateral stumps of cartilages were then trimmed back to the costal junctions, and in some instances a portion of bony rib was removed because of angulation. An attempt was made to preserve most of the perichondrium and periosteum for regeneration. The portion of the ninth rib was then trimmed and fitted in place beneath the sternum. Different positions were tried, and the most satisfactory one was with the concave side upward and the periosteum-covered side down. The rib rested on the second rib on the right side, making a bridge beneath the sternum across to the third rib on the left (fig. 2). This position allowed a slight natural concavity in this region to remain. The periosteum was then reflected from the small area of the second rib (right) and the third rib (left) where the rib graft touched. The graft was then firmly anchored to these two ribs by means of wires passed completely around them.

The perichondrium from the cartilages that had been excised was picked up and anchored to the border of the sternum in its natural location. The fascia of the rectus abdominis muscle was sutured to the lower end of the sternum. Before completely closing the wound, the anesthetist inflated both lungs with positive pressure until it was seen that the dead space beneath the sternum was entirely filled. The wound was then closed completely with no drainage while this positive pressure was being maintained. An ordinary dressing was applied in the usual manner, using "elastoplast" tape.

The rib graft was an osteoperiosteal one, with the anterior covering of periosteum left attached to the rib. Whether this is important or not is not known; however, after four years the rib is still in place and appears solidly fused on both sides and to the sternum. Figure 3 shows no shrinking or loss of substance in the graft. Dr. Herbert Adams suggests use of a rib from the bone bank. If such bone would remain viable, it would certainly simplify the procedure. In removing the cartilages, preservation of as much of the perichondrium as possible was attempted. Here also use of an osteotomy might be helpful; however, in this case the cartilages were so deformed that they were merely removed, and the result was excellent. The sternum in this case was flat. However, if a concave sternum should be encountered, an osteotomy on the under surface would be helpful, as proposed by Adams.[7] The rib strut was placed in different positions and left where it held the sternum elevated properly. In this case one end was placed across the second rib, whose cartilage was still attached to the sternum, and the other end of the strut on the anterior end of the third rib on the opposite side, the cartilage of which had been removed. The rib was simply anchored by

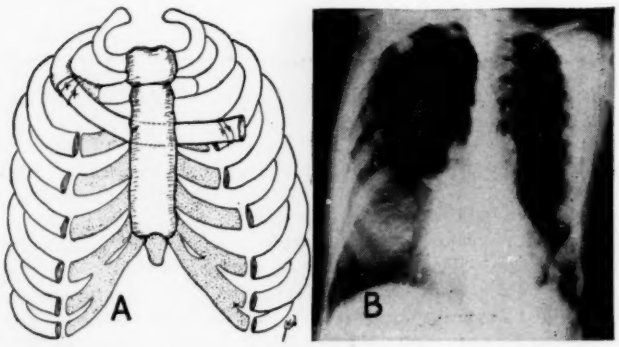

Fig. 2.—*A*, diagram of rib strut in place. *B*, oblique roentgenogram showing rib graft in place.

means of encircling wires. Drill holes were not used, and the strut was not anchored in any way to the sternum. Drilling holes for the wires in the rib ends, however, would fix them more securely.

The postoperative course was uneventful, this patient being ambulatory in six days. Three aspirations were performed to remove an accumulation of bloody serum beneath the sternum. Use of closed catheter suction would probably have been more helpful. Electrocardiographic studies show that the electrical cardiac axis has undergone a change from extreme right axis deviation (approximately 140 degrees) to a normal axis of 60 degrees. The auricular electrical axis also underwent a change, as indicated by a reduction in the amplitude of the P wave from 3 to 1½ mm. After four years there is still a perfect anatomical and functional result of the use of this technique.

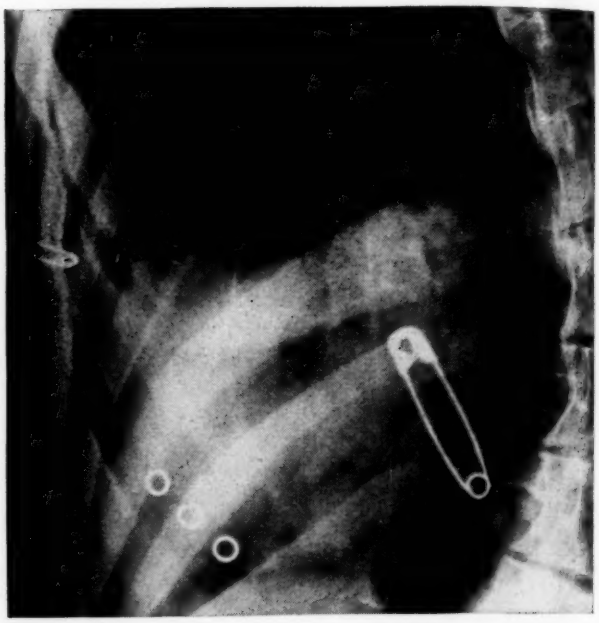

Fig. 3.—Roentgenogram made four years postoperatively shows no shrinkage or loss of substance in the graft.

SUMMARY

The symptoms produced by the funnel chest deformity and the reasons for correcting it are discussed. Ochsner and DeBakey's review of the literature and grouping of the many operative procedures previously devised to correct funnel chest deformity are discussed. The cases are divided into two age groups: the age group before 24 months in which a simple operation can be done and the patients older than 24 months in whom the deformity is fixed and the more extensive procedures are necessary. A new technique is proposed for repair of pectus excavatum, using a substernal osteoperiosteal rib graft as a strut in the older age group.

A case illustrating the procedure, which is described in detail, is discussed and illustrated by diagram and roentgenograms, showing the preoperative condition and the results four years after operation.

Evidence is shown that an osteoperiosteal bone graft (rib) used to bridge a wide gap remained completely fused and functioning after four years, with no loss of structure or change. This might suggest use of such a graft in other orthopedic or plastic procedures where bridging a gap is necessary. Comparison of results using rib bone from a bank with and without attached periosteum would be interesting.

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ARSENOTHERAPY IN THE TREATMENT OF EOSINOPHILIC PNEUMONOPATHY

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The term "eosinophilic pneumonopathy syndrome" was introduced by Apley and Grant [1] in 1944 to describe the various conditions that present the combination of eosinophilia and pulmonary lesions. Under this term was included Loeffler's syndrome, tropical eosinophilia, bronchial asthma, periarteritis nodosa, and some intestinal infestations. Their contention was that the differentiation between Loeffler's syndrome and tropical eosinophilia was more apparent than real and that they should be considered as the manifestation of one type of disease process. Recently when Vines and Clarke [2] reported a case with eosinophilia and pulmonary infiltrations they employed this term because the disease could not be properly placed in any specific category. Greig [3] also regarded Loeffler's syndrome and tropical eosinophilia as identical diseases. The picture is further confused by the use of other terms to describe this combination. Reiman [4] described it as allergic pneumonia. Others have used pseudotuberculosis associated with eosinophilia,[5] Loeffler's syndrome, and eosinophilic lung.[6] This same combination has also been described in totally unrelated diseases, such as eosinophilic leukemia, sarcoidosis, pulmonary tuberculosis, brucellosis, and Hodgkin's disease. It has been described in numerous types of parasitic infestations, such as those caused by Endamoeba histolytica, Ascaris lumbricoides, Necator americanus, Distoma, Coccidiodes immitis, larvae causing cutaneous helminthiasis, Strongyloides stercoralis, Trichinella, and the mite, Acarina. Certain plant pollens have also been thought to be an exciting agent.

There have been extensive reports that demonstrated the effectiveness of corticotropin (ACTH) and cortisone in the treatment of eosinophilic pneumonotherapy under the heading of Loeffler's syndrome.[7] There are few reports concerning the use of arsenic in this syndrome. The reports that are available have been found with few exceptions in the foreign literature describing the treatment of tropical eosinophilia.[8] It has been only recently that tropical eosinophilia has been described, and all cases have occurred in the Orient or in persons having returned from that region. In 1943, Weingarten [8f] reported 81 cases in persons from the western seacoast of India. In 1943, Simeons [5a] reported 35 patients from Bombay and termed the condition pseudotuberculosis of the lungs with eosinophilia. Treu [5b] described the disease in Calcutta. In England Apley and Grant [8g] described five cases seen in patients who returned from the Far East with pulmonary diseases. In the American literature two cases in Indian natives were reported by Hodes and Wood [6] while stationed at an army hospital in India. Nothing definite is known concerning the cause of eosinophilic pneumonopathy as it occurs in the tropics. It was by chance that Weingarten [8f] in 1936 discovered the effectiveness of arsenic in this condition. According to his description a patient under observation with tropical eosinophilia contracted syphilis. After the fourth injection of neoarsphenamine the subjective symptoms of his tropical eosinophilia vanished, his white blood cell count returned to normal, and the eosinophilia fell from 71 to 16%. The effectiveness of this form of therapy has been confirmed by others.[9] The case report that follows is intended to demonstrate the effectiveness of arsenotherapy in a native North American who presented asthmatic bronchitis, fever, eosinophilic leukocytosis, and pulmonary infiltration.

REPORT OF CASE

A 38-year-old white businessman was first seen in consultation on Aug. 7, 1950, because of intractable asthma. The patient had been hospitalized previously on July 29, 1950, complaining of severe cough, wheezing, and dyspnea of two weeks' duration. The patient had spent most of his life in the region of the gulf states but during the past two years had lived in the midwestern states. There were no hints in his past history to suggest an allergic disorder. His deceased father, however, had been known to have had a chronic nasal catarrh. The patient had been in good health until he was hospitalized on Jan. 30, 1950, for what was reported to be bronchopneumonia and bronchial asthma. The available hospital records revealed that while in Texas on

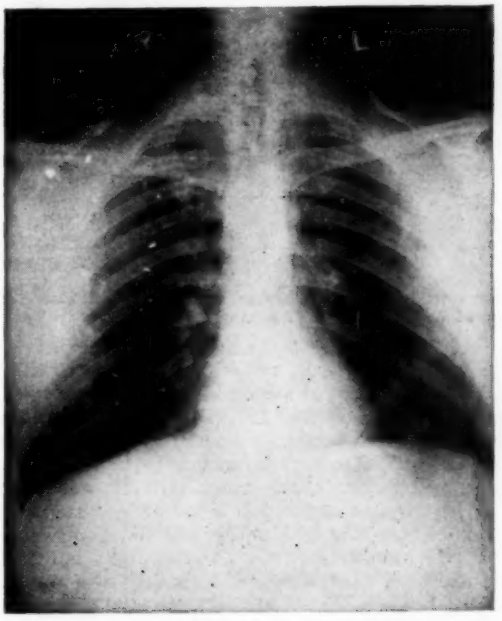

Fig. 1.—Roentgenogram on admission July 29, 1950, showing a diffuse finely mottled infiltration throughout.

a business trip he developed a "chest cold" on Jan. 20, 1950, for which he received a penicillin injection. His response was unsatisfactory, so two more injections of penicillin were given and an unknown amount of aureomycin added to the treatment. Although his recovery had not been complete he had improved enough so that he ventured a return airplane trip to the northern states on Jan. 29, 1950. At the completion of his trip he sought immediate hospitalization because of severe dyspnea.

Physical examination on admission revealed a well-developed, somewhat obese man with moderately severe respiratory dis-

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From the Department of Internal Medicine, Northwest Clinic.

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2. Vines, R. W., and Clarke, D.: Treatment of Eosinophilic Pneumonopathy: Report of a Case Treated with ACTH, New England J. Med. **244**: 826-829, 1951.

3. Greig, E. D. W.: Tropical Eosinophilia Associated with Pulmonary Signs (Loeffler's Syndrome), J. Trop. Med. **48**: 149-151, 1945-1946.

4. Reiman, in Cecil, R. L., editor: Textbook of Medicine, ed 7, Philadelphia, W. B. Saunders Company, 1948, p. 961.

5. (*a*) Simeons, A. T. W.: Pseudo-Tuberculosis of Lungs with Eosinophilia, correspondence, Indian M. Gaz. **78**: 271-272, 1943. (*b*) Treu, R.: Pseudo-Tuberculosis of the Lungs with Eosinophilia: Contribution to Treatment, ibid. **78**: 70-71, 1943.

6. Hodes, P. J., and Wood, F. C.: Eosinophilic Lung (Tropical Eosinophilia), Am. J. M. Sc. **210**: 288-295, 1945.

tress. The temperature was 99 F, pulse 108, and respirations 38 per minute. The blood pressure was 130 mm. Hg systolic and 90 diastolic. The only positive physical finding noted at this time was numerous inspiratory and expiratory musical rales throughout all lung fields. The laboratory examinations were as follows: red blood cell count, 5,620,000; hemoglobin, 18 gm.

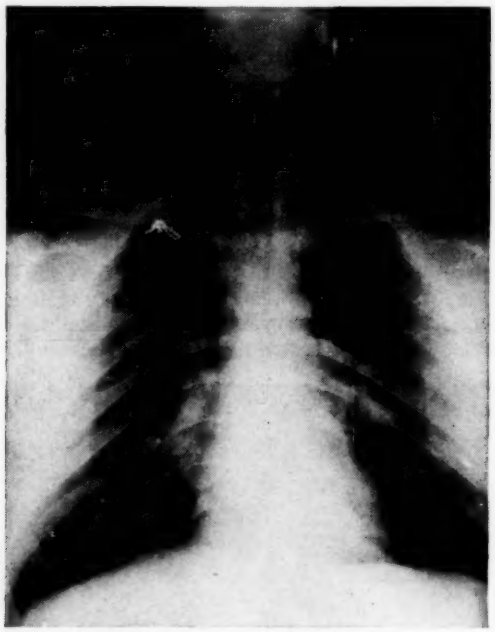

Fig. 2.—Roentgenogram on Aug. 5, 1950, showing an increase of the parenchymal infiltrations especially in the midportions. Coarse nodular infiltrations have become evident in the hilar regions.

(photocolorimetric method); and white blood cell count, 20,500 with a differential count of neutrophils 74%, lymphocytes 21%, eosinophils 3%, and basophils 2%. A urinalysis showed a specific gravity of 1.028, acid reaction, a trace of albumin, no sugar, 1 to 3 hyaline casts, and 2 to 4 white blood cells per high power field. A roentgenogram of the chest on Jan. 31, 1950, was reported as follows. There was some increase in both hilar shadows. In the midportion of both lung fields and in both lower lobes there was a diffuse finely mottled infiltration. The cardiac silhouette, mediastinum, and bony structures were normal.

Immediately upon admission to the hospital the patient was placed in an oxygen tent. He was given sedation, antihistamines, aminophylline suppositories, cough syrup, and aureomycin therapy. He gradually improved and was discharged asymptomatic on his 11th hospital day. Throughout his hospital course the temperature remained normal.

His second hospital admission began on July 29, 1950, because of cough and shortness of breath. In the interval between admissions to the hospital he had complained of malaise and a slight persistent nonproductive cough. One week before admission while driving along a dusty country road he again experienced dyspnea, wheezing, and paroxysms of cough. During the next few days these symptoms persisted but were less severe. The cough had become productive of small amounts of white frothy sputum. During the day previous to admission he had an exacerbation of his respiratory symptoms and was required to sit up to get his breath. During this week he was seen on several occasions by a physician who reported a low grade fever. There was no evidence from the past history that he had been exposed to any industrial or household chemicals. He had at no time been outside the borders of the continental United States. There was no history of a skin disorder, gastrointestinal symptoms, or direct exposure to cattle.

Physical examination showed a temperature of 98 F, pulse 80, respirations 22, and blood pressure 110 systolic and 70 diastolic. The patient was a short, stocky, somewhat plethoric appearing man in moderate respiratory distress. Typical asthmatic type of respirations were audible throughout the room. The patient was somewhat apprehensive, and increased sweating was evident. His color was good. There were no eruptions of his skin. Examination of the eyes, fundi, nose, ears, throat, and thyroid gland was without noteworthy change. There was no palpable enlargement of any lymph glands.

The chest was symmetrical, and expansion was adequate and equal. The percussion note throughout the lungs was normal. Throughout all lung fields there were numerous loud inspiratory and expiratory musical rales typical of bronchial asthma. There were no signs of consolidation. The left border of cardiac dulness was 9.5 cm. from the midsternal line in the fifth intercostal space. The rhythm was regular. The sounds were of good quality, and there were no murmurs, gallop, or friction rubs audible. The aortic and pulmonic second sounds were of approximately equal intensity. Examinations of the abdomen, genitalia, rectum, extremities, and neurological system revealed no noteworthy changes.

The laboratory examinations were as follows: red blood cells, 5,440,000; hemoglobin, 17 gm.; and white blood cells, 12,600, with a differential count of 58% polymorphonuclears, 12% lymphocytes, 28% eosinophils, and 2% basophils. Urinalysis showed an acid reaction, specific gravity of 1.005, no sugar, no albumin, and a rare white blood cell count per high power field. The serologic examination was negative. A sedimentation rate (Wintrobe method) was 13 mm. in one hour. The total serum protein was 6.05 per 100 cc.; serum albumin, 4.34 gm. per 100 cc.; and serum globulin, 1.71 gm. per 100 cc. Sputum smears

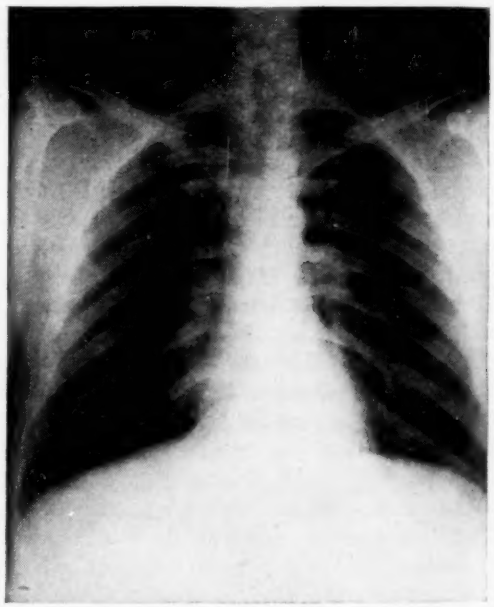

Fig. 3.—Roentgenogram on Aug. 14, 1950, after two injections of neoarsphenamine showing complete clearing of the infiltrations.

from 24 hour collections on two occasions were negative for acid-fast bacilli. Stool examinations on two occasions were negative for parasites. Roentgenography of the chest on admission (fig. 1) showed a finely mottled infiltration of almost uniform density throughout both lungs except at the apices. The hilar shadows, mediastinum, cardiac shadow, and bony structure were normal. X-ray examination of the skull, pelvis, and left hand showed no evidence of bone disease.

7. (*a*) Vines and Clarke.[2] (*b*) Herbert, P.; deVries, J. A., and Rose, B.: Studies on Effect of Administration of Pituitary Adrenocorticotrophic Hormone (ACTH) to Case of Loeffler's Syndrome and Case of Tropical Eosinophilia, J. Allergy **21**: 12-24, 1950. (*c*) Rose, B.: Studies on the Effect of ACTH on Eosinophilia and Bronchial Asthma, in Proceedings of the First Clinical ACTH Conference, edited by J. R. Mote, 1950, Philadelphia, The Blakiston Company, pp. 491-504. (*d*) Bordley, J. E.; Harvey, G. M.; Howard, J. E., and Newman, E. V.: Preliminary Report on the Use of ACTH in Hypersensitive State, ibid. pp. 469-478, 607.

8. (*a*) Apley and Grant.[1] (*b*) Greig.[3] (*c*) Simeons.[5a] (*d*) Treu.[5b] (*e*) Hodes and Wood.[6] (*f*) Weingarten, R. J.: Tropical Eosinophilia, Lancet **1**: 103-105, 1943. (*g*) Apley, J., and Grant, G. H.: Tropical Eosinophilia as Seen in England, ibid. **1**: 812-813, 1945.

9. Apley and Grant.[1] Hodes and Wood.[6] Apley and Grant.[8g]

On admission to the hospital the patient was given aminophylline suppositories, antibiotics, mild sedation, and antihistamines. On occasions of severe paroxysms of cough and dyspnea, oxygen therapy and small doses of morphine were required. Occasionally injections of epinephrine (adrenalin®) would afford some relief. Although these measures gave temporary relief there was no great change in his general condition. During his fourth, fifth, and sixth hospital days he ran a low grade fever.

A repeat chest film on Aug. 5, 1950, (fig. 2) revealed an increase of the previously described infiltration in the midportion of both lung fields. In addition, the hilar shadows showed enlargement with coarse nodular lesions. On Aug. 9, 1950, he was given his first injection of neoarsphenamine, 0.15 gm. intravenously. A blood cell count on this date showed a white blood cell count of 10,750 with 45% polymorphonuclears, 28% lymphocytes, and 27% eosinophils. The following day a chest roentgenogram revealed some decrease in the parenchymal and hilar infiltrations. On Aug. 11, 1950, a bronchoscopy was performed. The mucous membrane of the trachea and large bronchi showed a generalized swelling and redness. There were no masses or ulcerations observed. The passages contained only a moderate amount of clear mucoid secretion. A smear of this secretion revealed a very few organisms, no acid-fast bacilli, and 24% eosinophilia. Cultures for acid-fast bacilli and fungi were made and subsequently reported as negative.

On Aug. 13, 1950, the patient first noted a decrease in the number and severity of his asthmatic paroxysms. He was then given neoarsphenamine, 0.3 gm. intravenously. During the next three days he improved dramatically so that no further treatment was necessary. Examination of the chest revealed a marked decrease in the number and intensity of the asthmatic sounds. He was discharged on Aug. 16, 1950, with instructions to report to his family physician for two more neoarsphenamine injections of 0.3 gm. each at four day intervals. A recheck chest roentgenogram on Aug. 14, 1950, (fig. 3) showed complete clearing of the pulmonary infiltration. A white blood cell count was 11,750, with 54% polymorphonuclears, 18% lymphocytes, 1% monocytes, 24% eosinophils, and 3% basophils. Although direct examination has not been possible since his discharge, word from his local physician reveals that there was a complete remission of his symptoms for four months. At this time he again experienced a mild attack, which was promptly relieved by a single injection of neoarsphenamine. Over a year's time there have been three further attacks, each of which has responded to neoarsphenamine.

COMMENT

The term eosinophilic pneumonopathy syndrome was used in describing this case since its manifestations overlapped the descriptions of Loeffler's syndrome, tropical eosinophilia, and bronchial asthma. Loeffler's syndrome is described as a mild, self-limited disease with few symptoms. There may be a low grade fever and a slight irritative cough. Asthmatic attacks are said to be rare. It occurs only in dry, temperate regions. In contrast to tropical eosinophilia there is less leukocytosis and less eosinophilia; the pulmonary lesions have a different pattern, and they change rapidly. The typical clinical picture of tropical eosinophilia consists of a pronounced eosinophilic leukocytosis, fever, asthmatic bronchitis, and a diffuse mottling and soft nodulation throughout both lungs. Some observers have reported splenomegaly to be seen in a high percentage of patients. It is a chronic disease that occurs only in damp tropical climates. Confirmation of the diagnosis is made by its response to arsenic treatment. In the description of uncomplicated bronchial asthma a marked eosinophilia, fever, and pulmonary infiltration are not included. There are exceptions, however.

Any attempt to classify the case presented here as being specifically Loeffler's syndrome, tropical eosinophilia, or bronchial asthma meets with difficulty. It resembles Loeffler's syndrome in that there was little or no fever, a moderate eosinophilic leukocytosis, a pulmonary infiltration, and the fact that it occurred in a native North American who had never been in the tropics. It resembled tropical eosinophilia in that its course was chronic, the symptoms were severe, there was typical asthmatic bronchitis, and treatment with neoarsphenamine was effective. It resembled bronchial asthma by its pulmonary signs and symptoms.

Until the etiology of these conditions can be discovered or a more clear-cut clinical picture differentiated, it would be reasonable to include all cases presenting eosinophilia and pulmonary infiltration under the general heading of the eosinophilic pneumonopathy syndrome. The syndrome could then be subdivided into three major categories: those of unknown etiology, those of known etiology, and those associated with other diseases. A classification could be proposed as follows: (1) unknown etiology—Loeffler's syndrome, tropical eosinophilia, and bronchial asthma; (2) known etiology—parasitic infestations and plant pollens; and (3) associated with other diseases—eosinophilic leukemia, sarcoidosis, pulmonary tuberculosis, brucellosis, and Hodgkin's disease.

Although it is only speculation, perhaps a better insight could be gained into the relationship of Loeffler's syndrome and tropical eosinophilia if arsenic therapy would be given a trial in Loeffler's syndrome. On the other hand, Herbert, deVries, and Rose [7b] have reported the only case of tropical eosinophilia treated with corticotropin. They recorded a poor response. Their method of treatment, however, was inadequate so that a more thorough and extensive trial would be of great theoretical and practical interest.

SUMMARY

A case report is presented that was characterized by asthmatic bronchitis, eosinophilic leukocytosis, and pulmonary infiltration. Since the features of this illness resembled Loeffler's syndrome, tropical eosinophilia, and bronchial asthma, the term eosinophilic pneumonopathy syndrome has been employed. This illness was effectively treated with neoarsphenamine.

20 Fourth Ave., S. W.

Vitamin D and Rickets.—An outstanding contribution to knowledge of vitamin metabolism has been made by Zetterström and his collaborators, who have studied the role of vitamin D in enzymatic reactions. Utilizing a water-soluble phosphorylated vitamin D_2, they have demonstrated that vitamin D activates alkaline phosphatases of bone, kidneys, and intestine, this effect being particularly marked in the case of bone phosphatase. Thus, an enzymatic explanation of the role of vitamin D in the prevention of rickets is provided. Alkaline phosphatases are believed to have a role in intestinal absorption, renal tubular reabsorption, and the deposition of phosphate in bone. If these phosphatases need to be activated by vitamin D, a deficiency of this vitamin will result in poor intestinal absorption, excessive renal loss of phosphates, and poor ossification, the three essential aspects of rickets.—Goldsmith, G. A., Unglaub, W. G., and Bibbens, J.: Recent Advances in Nutrition and Metabolism, *A.M.A. Archives of Internal Medicine* **90**:513 (Oct.) 1952.

SIMPLE CLINICAL AID IN DIAGNOSIS OF HEMORRHAGIC PERICARDIAC EFFUSION

Clarence W. Mills, M.D., Atlanta, Ga.

The problem of differentiating grossly bloody fluid in the pericardiac sac from intracardiac blood during a pericardicentesis may sometimes be difficult. Fortunately, this situation seldom occurs, but, when it does, it is usually in a patient who is acutely ill and can poorly tolerate loss of an appreciable quantity of blood as the result of unintentional aspiration of blood from the heart. In the following abridged case report, such a distinction was rendered difficult by the anatomic changes caused by the underlying disease and the effects of therapy. The use of

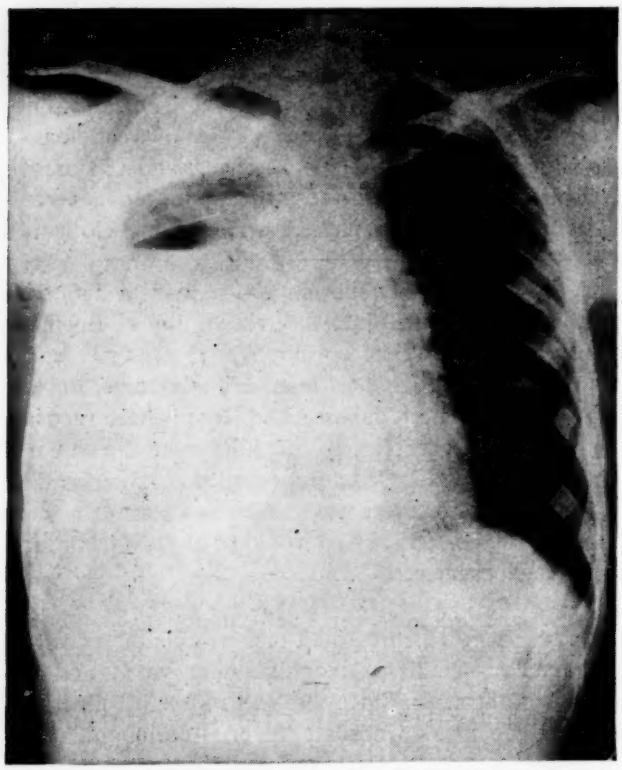

Fig. 1.—Roentgenogram made Nov. 26, 1951,

the procedure described below as an aid in determining the source of the blood obtained at pericardicentesis was arrived at by fortuitous circumstances, and its simplicity was sufficiently appealing to warrant publication.

REPORT OF A CASE

A 17-year-old white boy had an extensive lymphoblastic lymphoma of the mediastinum and right pleura of three months' duration at the time of hospitalization. As a result of prolonged serosanguineous right pleural effusion, the right pleura was considerably thickened and the underlying lung markedly collapsed (fig. 1). These changes accounted for an appreciable degree of exertional dyspnea which, as the pleural fluid accumulated between aspirations, would temporarily increase in severity; he also exhibited the postural aggravation characteristic of orthopnea. X-ray radiation and nitrogen mustard therapy were employed with brief benefit.

On one occasion, one week after a course of nitrogen mustard therapy, epistaxis and subcutaneous ecchymoses occurred as a result of secondary pancytopenia. At the same time, a moderate tachycardia and increase in exertional and postural dyspnea developed; this was thought to be partly caused by the rapid development of anemia as measured by a decrease in hemoglobin from 12 gm. per 100 cc. of blood to 7 gm. per 100 cc. during this period (Sahli method). Concomitantly, increasingly severe orthopnea developed. The patient was hospitalized. A teleroentgenogram of the chest revealed only a slight increase in cardiac silhouette size and no change in contour; the pleural fluid had not reaccumulated to an excessive degree (fig. 2). The blood pressure remained at a constant level, averaging 110 mm. Hg systolic and 70 mm. Hg diastolic; a paradoxical pulse was not detected. No rales were heard in either lung. The superficial neck veins on both sides became slightly distended whenever the patient assumed a semirecumbent position, and this sign increased to a point at which venous distension was present when he was in an upright position. Fluoroscopic examination of the chest revealed a diminution, but not an absence, of the cardiac pulsation. Circulation time was determined, using 10 cc. of 10% calcium gluconate intravenously, and was found to be 16 seconds. A tentative diagnosis of spontaneous pericardiac effusion was made, although the findings did not rule out the possibility of cardiac dilatation.

Exploratory pericardicentesis was elected, and the skin puncture site was selected 2 cm. lateral to the left sternal border in the fourth intercostal space. Gross blood was encountered at a depth of 3 cm. from the skin surface and was indistinguishable from a specimen drawn shortly before from an antecubital vein. It occurred to me that the patient had just become familiarized with the end point sensation of a calcium gluconate circulation time determination, and it seemed logical that an injection of the same chemical into the space from which the grossly bloody fluid was obtained would quickly determine whether the needle tip was within the cardiac chamber by the relatively prompt presence or absence of the characteristic end point sensation. A 10 cc. volume of 10% calcium gluconate was injected. Inasmuch as no end point was experienced during a period of two minutes after injection, it was concluded that the needle tip was not in a cardiac chamber, and 500 cc. of gross blood were withdrawn. No immediate ill effects were observed, and within a few minutes obvious relief of symptoms caused by a moderate degree of cardiac tamponade was noted.

The clinical improvement following the aspiration of the accumulated pericardiac blood was short-lived, however, because of progression of the underlying disease. Death occurred three weeks later. Postmortem examination revealed, in addition to the clinically recognized pleural and mediastinal disease, that the lymphoma had extended, so that it surrounded the pericardium almost completely with a firm 1 to 3 mm. thickness of tumor tissue.

COMMENT

The occurrence of spontaneous pericardiac hemorrhage in sufficient quantity to produce signs and symptoms of cardiac embarrassment was masked by preexisting changes caused by a mediastinal and pleural lymphoma. Pericardiac and pleural involvement by tumor infiltration had produced sufficient rigidity to prevent the appearance of the characteristic shape of the cardiac silhouette usually seen in the roentgenogram of a pericardiac effusion in excess of 200 or 300 cc. Hemorrhage into the pericardiac sac occurred at the time when other generalized bleeding manifestations of nitrogen mustard toxicity were taking place; it was assumed that this was another site of bleeding, but the presence of the tumor tissue in the pericardium, in retrospect, permits the possibility of a spontaneously bleeding tumor. The dilemma of encountering gross blood at exploratory pericardicentesis was satisfactorily resolved by the application of a well-established method for the determination of blood circulation time.

The same technique could be employed in a comatose or uncooperative patient by using a chemical such as sodium cyanide, the endpoint of which is of an objective nature. In considering the situations that may produce misleading results, it appears that a condition involving an actual physical communication between an intracardiac chamber and the pericardiac sac would be necessary; it is obvious that a rapidly, and probably fatal, developing cardiac tamponade would serve to distinguish a situation in which a sizeable communication existed, and this technique would be unnecessary. Were the communication small or valvular in function, it is conceivable that small quantities of the chemical might find its way from the pericardiac sac into a cardiac chamber despite the immense pressure gradient that would exist between the two spaces. Otherwise, it seems as if this technique would

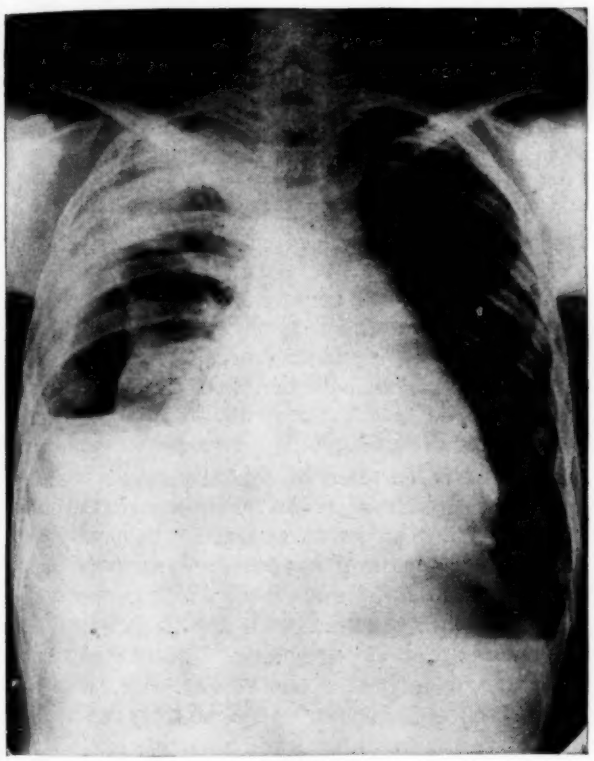

Fig. 2.—Roentgenogram made Dec. 31, 1951.

be reliable in determining the source of blood obtained at exploratory pericardicentesis when the clinical differentiation of bloody pericardiac effusion and cardiac dilatation could not definitely be made.

SUMMARY

A case report is described wherein the injection of a 10% calcium gluconate solution through an exploratory pericardicentesis needle was helpful in determining the source of gross blood obtained initially through the aspiration needle. The rationale of the procedure and the possibilities of misleading results are discussed. It is recommended that each instance of initial pericardicentesis be preceded by a circulation time determination, so that advantage may be taken of the above-described technique if the situation necessitates clarification.

384 Peachtree St.

EXPERIENCES WITH THE MURLESS HEAD EXTRACTOR IN CESAREAN SECTION

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and
Salvatore R. Carrabba, M.D., New York

In 1948, Murless, of Durban, South Africa, reported in the *British Medical Journal* [1] on the use of a new head extractor in low-segment cesarean section. He devised an original single-blade instrument, which he used in 100 low-flap operations to good advantage. Murless suggested that his blade be tried by others and improved, if necessary, so that its "routine use will simplify what most surgeons still regard as a difficult manoeuvre."

Accordingly, one of us (A. I. W.) wrote to Murless, and arrangements were made to obtain one of his extractors through the inventor's assistance. In late 1950, the instrument arrived from England,[2] and its use was evaluated on our service in a large New York City hospital. Our experience with this apparatus is reported herewith.

The extractor is a single-blade fenestrated instrument, which at first glance would appear to be a cross between the blade of an ordinary obstetric forceps and a luggage handle. Actually, its unique S-shaped appearance does give the immediate impression that its usefulness would be applicable to a lifting action on the fetal head (fig. 1). The blade portion is, in fact, similar to the ordinary obstetric outlet blade except that it possesses an exaggerated cephalic curve. At the base of the blade is a double hinge, thus converting the forceps into a single eter of the shaft. The shaft, which connects the blade to the handle, carries a sliding sleeve. When this sleeve is placed into position, it covers the joint and locks the double hinge, thus converting the forceps into a single rigid piece (fig. 1). The "break" in the shaft accomplished by the double hinge allows for the introduction of the extractor, which would otherwise be impossible, owing to the obstructing pregnant uterus in the anterior abdominal wall.

Murless' original technique consists of making an initial 2-in. (5-cm.) transverse incision into the lower uterine segment. He then inserts the folded extractor between the lower edge of the incision and the fetal head; as the blade slides under the head the handle is straightened and the hinge locked. With an assistant holding the extractor to maintain pressure of the fetal head against the anterior uterine wall, the head is delivered slowly by fundal pressure as the surgeon enlarges the initial uterine incision bit by bit. Murless stated that in this manner bleeding is minimal and uterine tears negligible. Murless also pointed out that the head can be lifted out in any position and that the skull is subject to a minimum of pressure, probably less than in normal labor.

From the Department of Obstetrics and Gynecology of the New York Medical College and the Metropolitan Hospital, Dr. Clair E. Folsome, Director.

1. Murless, B. C.: Lower-Segment Caesarean Section: A New Head Extractor, Brit. M. J. **1**: 1234, 1948.

2. The original Murless extractor may be obtained through Allen and Hanburys, Wigmore St., London, England.

In our use of the Murless extractor, we were not concerned with the usual small amount of controllable bleeding, prior to delivery of the head, and consequently omitted making the initial 2-in. incision. Instead, we made our usual transverse incision, inserted the extractor, and delivered the head in accordance with the balance of Murless' instructions. In the event that further lateral incisions of the uterus were necessary, the line of incision was in full view at all times, owing to the lifting action of the extractor.

PRESENT STUDY

The Murless head extractor was used in 40 unselected patients in whom low-segment cesarean section was considered the method of choice. Among the 40 cases, there were 14 repeat cesarean operations, in which section was performed prior to the onset of labor. The remainder were initial low-flap operations. Of these, 21 were performed for cephalopelvic disproportion. Most of the patients were subjected to a preliminary test of labor. In three cases section was performed for prolonged labor associated with cervical dystocia, and in two section was done for placenta previa.

The locations of the presenting parts are of interest. Nineteen were found floating, 15 were just engaged, 4 were deeply engaged, and 2 were deeply impacted in the occiput transverse position. The presentation and positions were as follows:

Vertex presentations, oblique positions	28
Vertex presentations, transverse position	10
Breech presentations, left sacroanterior	2
Total	40

The weights of the babies varied from 4 lb. 2½ oz. (1,885 gm.; one of a set of twins) to 9 lb. 12 oz. (4,423 gm.). The average weight of the babies delivered by the Murless extractor was 7 lb. 4 oz. (3,289 gm.).

TECHNIQUE

The following technique was employed in each of the 38 vertex presentations. (The procedures with the two breech presentations are of interest and will be taken up later.) The abdomen was opened in the usual manner by a midline vertical incision. The vesicouterine peritoneal reflection was incised transversely and reflected down out of the field. An initial transverse incision was made in the lower segment with a scalpel and carried laterally by ordinary bandage scissors. The extractor was then introduced in the following manner.

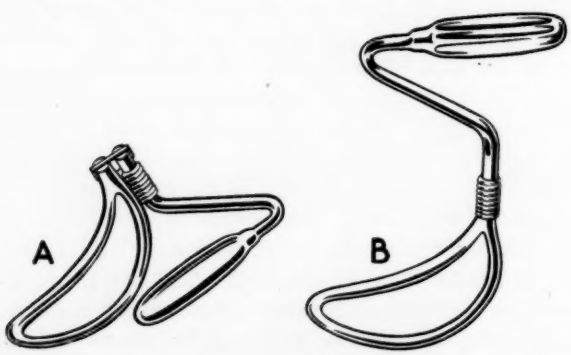

Fig. 1.—The Murless head extractor. *A*, in the folded position for insertion. *B*, in the rigid position for extraction of head.

Two fingers of the operator's left hand are placed in the uterine cavity just under the rami of the pubic bones. The presenting part is palpated and its position ascertained. The extractor is inserted with the right hand, being held in the folded position (fig. 2) until it envelops the fetal head. The handle of the blade is then elevated and the sleeve of the shaft depressed to lock the hinged joint (fig. 3 and 4). In no instance was it found necessary to change the position of the fetal head in order to secure the placing of the extractor. Regardless of the position of the head, the blade of the extractor was always placed directly in the midline curving under the head. (In this series no case of a direct occiput-anterior position was encountered; even if such a position would have been found, we would not have hesitated to apply the blade directly over the face. No compression is obtained when a single blade is utilized.)

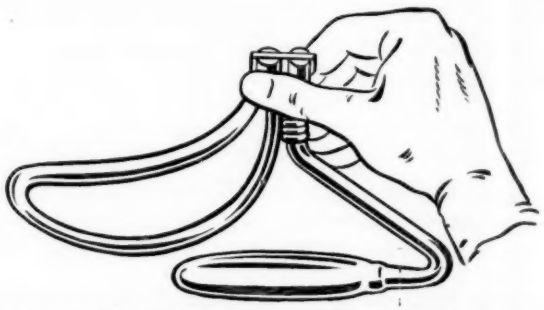

Fig. 2.—Method of holding extractor when inserting into uterus.

The head is delivered by fundal pressure while the operator gently and slowly lifts the head out of the uterus. Delivery is slow unless an emergency demands speed. It should be emphasized that delivery is accomplished by the assistant at the fundus while the operator merely guides the baby's head out of the uterine incision. There is no need to exert strong pulling effort on the extractor if the uterine incision is sufficiently wide. If a tight squeeze is encountered, the lateral incisions can be easily extended before the lifting action is completed. (Delivery in the transverse position was accomplished just as easily as from the oblique position.)

In the cases in which deep engagement or impaction was met, it was necessary to disimpact the head first before inserting the extractor. This is achieved by inserting two fingers into the uterine cavity and pushing the head up. "While the fingers are holding the head the instrument is introduced between the fingers and the lower edge of the uterine incision and slid into position before the fingers are withdrawn" (Murless).

Murless makes no mention of the use of his extractor in breech presentations. In this series, two breech deliveries were effected with the use of the Murless apparatus. In one frank breech, the extractor was inserted under the buttocks and the breech delivered just as simply as the fetus was lifted out of the uterus in vertex presentations. In the other breech case, the delivery was effected by extracting the feet manually, delivering the breech and shoulders in the same fashion, and then apply-

ing the Murless extractor to the after-coming head located at the incisional area. While we do not advocate the use of the head extractor for general use in breech presentations at section, the fact that it is useful in this connection adds to the value of the apparatus.

RESULTS

Forty deliveries at low-segment cesarean section were carried out with the Murless extractor. No complication of bladder, rectum, or other viscus was encountered. No tear of the uterus was noted. No maternal morbidity ascribable to use of the extractor was found. On the other hand, all the babies were born alive and well. No marks were found on the fetal head from the fenestrated blade. No evidence of cerebral damage to the infants was found after careful examination. No difficulty was encountered with the use of the extractor except for the fact that a few seconds were required for locking the sleeve. This was subsequently overcome with a modification of the shaft.[3] The average time consumed from the beginning of the insertion of the extractor to delivery of the presenting part was 20 to 40 seconds. In two instances, when speed was most important (fetal distress), delivery of the head was accomplished in less than 10 seconds from the time of blade insertion.

COMMENT

There is no doubt that one can easily deliver at cesarean operation the vast majority of babies by simply scooping up the baby's head manually and delivering it. With this we have no quarrel. On the other hand, the knowledge of the use of the Murless extractor can be of great relief to the operator who occasionally finds that he cannot deliver the baby manually. From time to time most men find that delivery in the ordinary way becomes

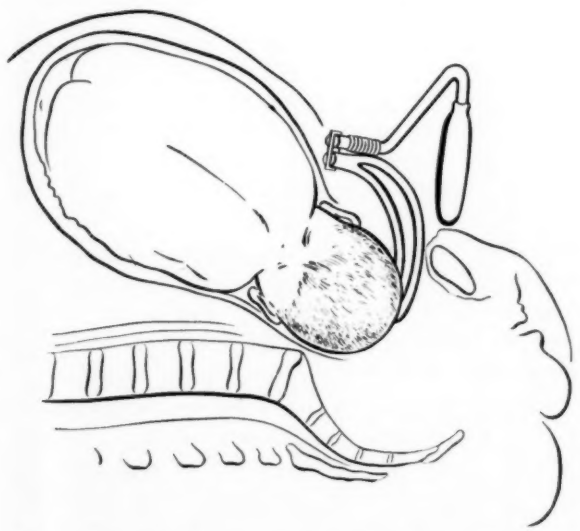

Fig. 3.—Schematic drawing illustrating path of Murless extractor.

rather difficult and will resort to using a pair of obstetric forceps, a vectis, or other means of delivering the head.

In such instances, particularly when the head is deeply engaged or when the head fits tightly in the pelvis, the manual method of delivery can now give way to an almost ideal method, use of the Murless extractor. We wish to point out, however, that unless the operator has had experience with the head extractor it should not be used in a difficult case. In other words, if the operator desires to use the Murless extractor only on occasions, he should perfect himself in its use in the simple case, so that, when the more difficult one presents itself, he will not have to fumble and waste time. We advocate the use of the Mur-

Fig. 4.—Schematic drawing illustrating the position of the extractor just prior to lifting head. Note assistant exerting fundal pressure.

less blade routinely for residents and young obstetricians in the "easy case" in preparation for its real need in difficult cases. A knowledge of the use of the extractor, together with the assurance derived from its presence on the instrument tray, will save babies.

Although we have used the Murless extractor on only 40 patients, we have become so convinced of its usefulness that it can be found on the instrument tray for every cesarean section that we perform, whether we have need for it or not. We are satisfied with Murless' instrument and feel that his claims for it can be substantiated. It does allow for better vision of the operative field, and the incision can be enlarged as required, thus preventing tearing of the uterus. The head can be lifted out in any position without the need to rotate it for forceps application. The fetal skull is subjected to a minimum of pressure, since there is no counter pressure with the single blade. It is definitely a neater surgical procedure.

SUMMARY

The Murless head extractor for low-flap cesarean sections has been used on 40 unselected patients requiring this operation. The claims of the original reporter have been substantiated. The Murless head extractor diminishes the amount of bleeding associated with cesarean operations, allows for better visualization of the field, and prevents uterine tears. It is easy to use, it may be applied

3. With the technical assistance of Mr. John L. Marco, we have improved the original Murless extractor. The sliding sleeve would be somewhat troublesome at times, causing slight delays in setting of the instrument. The extractor with its modification of an automatic locking sleeve is now simplified so that the mere raising of the handle locks the shaft immediately. Murless writes that he is pleased to hear of the improved mechanism for holding the blade rigid (personal communication to the authors, Feb. 29, 1952). The Murless extractor (modified) may be obtained through Goodman-Kleiner Co., New York.

to the head in any position, and it exerts a minimum of pressure on the fetal skull. It is of inestimable value in difficult deliveries of the head, when manual efforts at delivery of the head have failed. Its routine use in low-flap cesarean operation is strongly urged.

1160 Fifth Ave. (Dr. Weisman).

MYOCARDIAL INFARCTION AS A POST-OPERATIVE COMPLICATION OF MAJOR SURGERY

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and
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Myocardial infarction is an uncommon but challenging postoperative complication. A review of the clinical and autopsy data of 15 patients studied at Memorial Center was made in an attempt to evaluate the setting in which this complication developed, possible precipitating causes, the diagnostic aspects, as well as the course and treatment. It was hoped to ascertain the method in which this postoperative complication might best be anticipated, prevented, and treated.

MATERIAL AND METHODS

The electrocardiographic tracings obtained during the period from January, 1948, to December, 1951, were reviewed, and those showing unequivocal evidence of acute myocardial infarction due to coronary occlusion following major surgical procedures were selected. The clinical charts of the patients whose electrocardiograms had been selected were studied. In addition, a survey of the postmorten protocols for the same period was made, and the clinical charts of the patients who, at necropsy, showed recent myocardial infarction with coronary occlusion following major surgical procedures were reviewed. No case was used in which the electrocardiographic findings were questionable or in which the diagnosis was made clinically but was not confirmed by electrocardiographic or postmortem examination. Although the exact incidence of coronary occlusion following operation at this hospital cannot be stated, it would appear to be well under 0.8%, since approximately 20,000 operations were performed during this four year period. The electrocardiographic criteria for the diagnosis of coronary occlusion of anterior and posterior myocardial infarction were those prepared by Wilson,[1] Master,[2] and Friedberg.[3]

General Information.—The patients were white and ranged in age from 43 to 78 years, with an average of 62 years. There were 11 men and 4 women. Table 1 lists the primary discharge diagnoses.

Preoperative Cardiac Status.—Five patients had no subjective or objective clinical evidence of heart disease. Using the criteria of the New York Heart Association, three patients had arteriosclerotic heart disease, four had hypertensive and arteriosclerotic heart disease, two had arteriosclerotic heart disease with healed myocardial infarction, and one had pulmonary heart disease. As adjudged by a 6 ft. chest roentgenogram, 3 patients had cardiac enlargement of a mild to moderate degree, 10 had normal cardiac silhouettes, and 2 patients had no preoperative chest x-ray study. Eight patients had well-established systolic hypertension (above 150 mm. Hg), and of these four had concomitant diastolic hypertension (above 90 mm. Hg). Two patients had the classical anginal syndrome. According to the functional and therapeutic classification of the New York Heart Association, the following distribution was encountered: four patients were in class IA, four in IB, four in IIB, two in IIC, and one in IIID. All the patients had preoperative hemoglobin values of 12.0 gm. or more (Sahli method) with an upper limit of 15.8 gm. Five patients had normal preoperative electrocardiographic tracings, which included bipolar and unipolar extremity leads and unipolar precordial leads. Of these patients, two had mild hypertension, no cardiac enlargement, and were classified IA and IB respectively; two had an apical grade 2 systolic murmur, normal size hearts, and were classified IIB; and one had kyphoscoliotic chest deformity with diminished pulmonary reserve and was classified IIB. Ten patients had abnormal tracings; of these, three patients were clinically classified IA, three IB, one IIB, two IIC, and one IIID. Five patients had been satisfactorily digitalized preoperatively; in three of these cases, digitalization was done just prior to the operation, and in two it had been done several months before the operation. The other patients received no preoperative cardiotonic medications.

TABLE 1.—*Primary Diagnoses Inducing Surgery*

Disease	No. of Cases
Epidermoid carcinoma of the larynx	4
Adenocarcinoma of the rectum	3
Epidermoid carcinoma of the cervix	1
Epidermoid carcinoma of the lip	1
Adenocarcinoma of the ascending colon	1
Fibrosarcoma of the neck	1
Adenocarcinoma of the sigmoid	1
Carcinoma of the pancreatic duct	1
Tuberculosis of the left kidney	1
Intestinal obstruction	1

Surgical Procedures.—All the operations performed were of major scope and are listed in table 2. Of the operations done, six involved the head and neck region, seven the abdominal area, and two the pelvic cavity. Five patients received pentothal sodium intravenously supplemented with continuous oxygen inhalation; one received pentobarbital (nembutal®) sodium and curare; six were given nitrogen oxide, followed by administration of an ether-oxygen mixture; two were given spinal anesthetics supplemented by pentothal sodium intravenously; and one patient received cyclopropane. The surgical procedure varied in duration from 1.5 hours to 10 hours with an average of 3 hours in length. All patients except three received blood during the operation with the maximum

From the Medical Service of Memorial Center for Cancer and Allied Diseases.

This article has been shortened by omission of the report of cases and the figures, which will appear in the authors' reprints.

1. Wilson, F. N., and others: The Precordial Electrocardiogram, Am. Heart J. **27**: 19-85, 1944.

2. Master, A. M.; Dack, S.; Field, L. E., and Horn, H.: Diagnosis and Treatment of Acute Coronary Diseases, J. A. M. A. **141**: 887-891 (Nov. 26) 1949.

3. Friedberg, C. K.: Diseases of the Heart, Philadelphia, W. B. Saunders Company, 1950.

amount administered being 3,000 ml. The average amount of blood given was 1,000 ml. Other fluids administered intravenously included 5% glucose in distilled water and/or 5% glucose in sodium chloride in the amounts from 0 in two patients to 2,500 ml. in one, with an average of 550 ml. during the operative period. On the average, each patient received a total of 1,550 ml. of intravenous fluid during surgery. Seven patients had uncomplicated operative periods, and auricular fibrillation developed in one patient and persisted postoperatively. Seven patients had blood pressure falls of 20 mm. or more Hg systolic and 10 mm. or more Hg diastolic, and of these six patients showed surgical shock during the operation.

Preinfarction Postoperative Period.—During this period the hemoglobin value ranged from 10.7 gm. to 18.6 gm. with an average of 15.0 gm. Five patients were given maintenance doses of digitoxin. One additional patient was digitalized on the day of operation because of postoperative pulmonary edema, and he was maintained on daily digitoxin thereafter. Quinidine sulfate was given to one patient because of auricular fibrillation. Six patients had uncomplicated courses immediately (first 48 hours postoperatively) following their operation. Pulmonary edema developed in one patient; in one patient there was evisceration; one had a persistent auricular fibrillation; one had azotemia; and three patients had persistent postoperative hypotension. The maximum amount of intravenous fluid any one patient received in any 24 hours postoperatively varied from 0 to 5,500 ml. with an average of 3,000 ml. of fluid intravenously. Seven patients did not ambulate prior to their postoperative myocardial infarction; four left their bed on the first postoperative day, two on the second, one on the fourth, and one on the fifth.

It was not always possible to establish definitely the time of coronary occlusion, but it is estimated conservatively that the myocardial infarction occurred in two patients on the operative day, two on the operative or first postoperative day, one on the operative to the second postoperative day, two on the operative to the fifth postoperative day, one on the second postoperative day, one on the fourth postoperative day, and one each on the 10th, 16th, 18th, 20th, and 22nd postoperative day respectively. In three cases persistent hypotension appeared to play a dominant role in precipitating the infarction, and in one auricular fibrillation was related to the occlusive episode. In 11 cases no predominant precipitating cause other than the operative procedure itself could be established to account for the myocardial infarction. Persistent postoperative hypotension was the primary and predominant clinical manifestation in four cases, congestive failure in two, substernal pain with or without radiation in four, marked dyspnea and hyperpnea at rest in one, arrhythmia in two, and sudden death in two. Eleven patients had anterior wall and four had posterior wall myocardial infarction. All patients, except the two who died, were put on bedrest and were given oxygen. Six patients received anticoagulants, three patients were digitalized because of associated mild congestive heart failure, and three patients received quinidine sulfate because of occasional ventricular extrasystoles.

Follow-up.—Two of the patients died of cancer, one 11 months and one 3 months postoperatively. Six patients died of heart disease. Of this latter group, one died of myocardial infarction on the operative day, one of myocardial infarction on the first postoperative day, one on the 12th, 20th, and 23rd postoperative day respectively, and one patient died in congestive heart failure on the 22nd postoperative day. Of the seven surviving patients, two were alive 3 years postoperatively and were classified functionally and therapeutically as IIB; one patient, 1½ years following his operation and myocardial infarction, was in class IIB; one, 1½ years postoperatively, was in IVE and was bedridden; one, classified IIB, was alive 1 year postoperatively and survived a second myocardial infarction unrelated to surgery 12 months after his operation; one patient was in class IIB 6 months postoperatively; and one patient recovered from her cardiac episode too recently to permit accurate follow-up evaluation. Of the six patients receiving anticoagulants following myocardial infarction, none died of heart disease and one died of cancer three months postoperatively. The immediate postoperative mortality,

TABLE 2.—*Types of Surgical Procedures Performed*

Procedure	No. of Cases
Abdominal-perineal resection	4
Right radical neck dissection and total laryngectomy	3
Total laryngectomy with partial glossectomy and esophagectomy	1
Excision of right commissure of mouth	1
Exploratory laparotomy with ileotransverse colostomy	1
Left radical neck dissection	1
Total pancreatectomy with resection of stomach and duodenum	1
Left nephrectomy	1
Radical node dissection with total cystectomy, total hysterectomy and vaginectomy bilateral ureterointestinal implants	1
Radical vaginal hysterectomy with bilateral salpingo-oophorectomy	1

namely, those patients not surviving six weeks following the coronary occlusion related to major surgery, was 40%. In the preoperative clinical evaluation, four patients were labeled clinically as good operative risks; of these, three survived the operation to which they had been subjected and one died of his myocardial infarction on the first postoperative day. Of those three patients adjudged clinically as poor operative risks, two survived the operation and one died postoperatively of the sequelae of the coronary occlusion. The other patients received no operative risk evaluation preoperatively. Of the six patients who died during the six week period following myocardial infarction, two patients had normal electrocardiographic tracings with sinus tachycardia; one had nodal rhythm; one had a tracing consistent with old healed posterior infarction; one showed depressed ST segment in leads 2 and 3; and one had low voltage in the bipolar extremity leads.

COMMENT

The differences between acute myocardial infarction developing in the postoperative period and that occurring at a time unrelated to surgery are of interest, although the present series is too small to permit any final conclusions. The percentages and figures discussed are, there-

fore, not to be considered statistically significant until a larger series can be collected.

Table 3 summarizes these differences, and it is noted that 27% of the present series were women as contrasted to a general incidence of from 7 to 17%.[4] The age distribution is similar.[5] The incidence of hypertension was 53% in the present group as compared with 71 to 74% as reported in the literature,[6] and cardiac hypertrophy was encountered in 23% as compared with a general incidence of from 34 to 60%.[7] Chest pain occurred as a primary clinical manifestation in 27% of our patients. This is appreciably less than the 97% incidence generally reported.[8] Levine [9] states that pain may be absent in the presence of myocardial infarction, and Jacobs [5a] observes that infarction complicating surgery and trauma is frequently painless. The sensorium and general postoperative status of the patients subjected to major surgical operations are such as to increase the pain threshold in part as a result of the use of narcotics, analgesics, and sedatives. Dyspnea was noted as a primary manifestation in only one patient, but it was found in nearly 50% of the nonsurgical group.[5a] One-third of the patients with postoperative coronary occlusion presented congestive failure as a primary manifestation of coronary occlusion or as a concomitant feature of the myocardial infarction as compared with a 33 to 35% general incidence,[6a] although in none was the heart failure the only clinical manifestation of infarction. The immediate mortality, defined as the incidence of death in the period of six weeks from the onset of the coronary occlusion, is 40%. The literature reports wide variations in the mortality statistics of patients with myocardial infarction unrelated to surgical procedures; Master [6b] reports 8%, Conner and Holt [4b] 16.2%, and Levine [9] 53% mortality. Considering the age group of the patients in the present reported series, the over-all immediate mortality is not out of keeping with that seen following coronary artery occlusion with myocardial infarction unrelated to major surgery.

TABLE 3.—*Comparison of Myocardial Infarctions Unrelated and Related to Surgery*

	Percentage of Women	Average Age	Percentage with Hypertension	Percentage with Hypertrophy	Percentage with Substernal Pain	Percentage with Dyspnea	Percentage with Congestive Failure	Percentage of Mortalities
Myocardial infarction unrelated to surgery.....	7-17	62	71-74	34-60	97	50	33-35	8-53
Myocardial infarction developing as a postoperative complication (Memorial Hospital, 1948-1951)	27	62	53	23	27	7	33	40
Myocardial infarction developing as a postoperative complication (Mt. Sinai Hospital, 1931-1937)	21	62	85	52	40	34	..	66

The series reported here can best be compared with a group of 35 cases of postoperative coronary artery "occlusion" reported from Mt. Sinai Hospital in 1936.[10] The latter, however, includes 12 cases of myocardial infarction that occurred following minor surgical procedures, such as spinal tap, paravertebral block, tracheostomy, and others done under local anesthesia; and the duration of the operations was from 10 to 15 minutes to two hours, with only 10 operations consuming more than one hour and none longer than two hours. Three cases of myomalacia in the absence of coronary occlusion are included. In the present reported series, all operations were of major surgical magnitude and all were done under general anesthesia; in duration, the operations varied from 1½ to 10 hours in length with an average duration of 3 hours. All patients had acute myocardial infarction according to the criteria previously listed.

In a comparison of the Memorial Center and the Mt. Sinai Hospital series, the majority of the postoperative coronary occlusions appeared in both groups during the first three postoperative days, 51.5% in the Mt. Sinai group and 60% in the Memorial Center group. The other infarctions occurred in this order: at Mt. Sinai, 11.4% in 4 to 7 days, 31.4% in 8 to 14 days, and 5.7% in 15 to 21 days; and at the Memorial Center, 6.67% in 4 to 7 days, 6.67% in 8 to 14 days, 20% in 15 to 21 days, and 6.67% in 22 or more days. The decreased incidence of shock (60% at Mt. Sinai Hospital, 40% at the Memorial Center) and lowered mortality in the present group can probably be explained by the free use of oxygen, antimicrobial agents, anticoagulants, intravenous fluids, and other modern therapeutic modalities that were not at hand formerly and that serve to prevent and resolve such complications as shock, pneumonia, anoxia, uremia, peritonitis, sepsis, and other complications.

The association of surgical operation and coronary artery occlusion has been noted for some time, and several cases of postoperative myocardial infarction have been reported.[11] Saphir and co-workers [12] pointed out that anesthesia and surgical procedures may precipitate coronary thrombosis and suggested that the cardiac status of patients in the fourth decade or later upon whom operation is contemplated should be carefully evaluated. Master and associates [10] gave evidence that operation precipitated myocardial infarction. 1. In one-half of the postoperative cases, the occlusion occurred within three days after the operation. 2. Coronary occlusion was rare among patients who were in medical wards for chronic disease. 3. The high incidence (5%) of postoperative myocardial infarction among all hospital cases of coronary occlusion made the incidence significant.

The mechanisms by which operations precipitate coronary occlusion are not clear, but the factors that play a

4. (*a*) Biand, E. F., and White, P. D.: Coronary Thrombosis (with Myocardial Infarction): 10 Years Later, J. A. M. A. **117**: 1171-1173 (Oct. 4) 1941. (*b*) Conner, L. A., and Holt, E.: The Subsequent Course and Prognosis in Coronary Thrombosis: Analysis of 287 Cases, Am. Heart J. **5**: 705-719, 1930.

5. (*a*) Jacobs, T. P.: The Initial Attack of Acute Myocardial Infarction, Ann. Int. Med. **34**: 114-140, 1951. (*b*) Levine, S. A., and Rosenbaum, F. F.: Prognostic Value of Various Clinical and Electrocardiographic Features of Acute Myocardial Infarction: Ultimate Progress, Arch. Int. Med. **68**: 1215-1231 (Dec.) 1941.

6. (*a*) Chambers, W. N.: Acute Myocardial Infarction: A Study of 100 Consecutive Cases, New England J. Med. **235**: 347-352, 1946. (*b*) Master, A. M.: Incidence of Acute Coronary Artery Occlusion: Discussion of Factors Responsible for Its Increase, Am. Heart J. **33**: 135-145, 1947.

7. Jacobs.[5a] Master, A. M.; Jaffe, H. L.; Dack, S., and Silver, N.: The Course of the Blood Pressure Before, During, and After Coronary Occlusion, Am. Heart J. **26**: 92-107, 1943.

8. Jacobs.[5a] Bland and White.[4a]

9. Levine, S. A.: Coronary Thrombosis: Its Various Clinical Features, Medicine **8**: 245-418, 1929.

role are: (1) preexisting coronary artery disease, (2) blood coaguability, (3) surgical shock and anoxia, (4) blood volume alterations, (5) tachycardia and/or arrythmia, and (6) others. Coronary artery occlusion is usually due to thrombosis on an arteriosclerotic plaque or possibly to hemorrhage inside the plaque and may be precipitated by alteration in the coronary circulatory dynamics. Although it is conceivable that coronary artery occlusion may occur postoperatively in the absence of any pathological alteration in the coronary vessels, such a possibility seems highly unlikely, with the exception of embolization. The role that blood coagulation plays in postoperative coronary artery thrombosis is somewhat obscure; tissue injury, increase in circulating fibrinogen, and blood platelets are considered by Evans to play a role.[13]

Surgical shock may be a precursor of myocardial infarction as a result of slowing of blood flow through coronary vessels and a decrease in mean coronary blood pressure with resulting tendency to clot formation.[14] Hemorrhagic shock is associated with a decrease in coronary blood flow of 30 to 60% with a concomitant decrease in flow resistance, probably as a result of coronary arterial dilatation.[15] Dehydration, like shock, is associated with a diminution in blood volume and an increase in viscosity of the blood, both of which tend to favor occlusion. The latent interval between surgical shock in those cases in which it is present and the appearance clinically of the coronary occlusion may be explained in two ways. 1. The thrombotic lesion in the coronary artery may be initiated during the shock period and thereafter may produce complete arterial occlusion either rapidly or slowly. 2. The thrombotic lesion may not develop during the period of shock but at a later time when the patient has recovered from shock.

Tachycardia with or without arrhythmia may produce coronary insufficiency by virtue of the shortened diastole and the increased oxygen need of the heart. The factors that do not appear to play a demonstrable role in precipitating postoperative coronary artery thrombosis include the type or site of operation, digitalization, and ambulation. Those factors that may be involved indirectly include anemia, anoxia, length of operation, anesthesia, noncardiovascular complications, excessive transfusions, and other intravenous fluids.

The diagnosis of coronary artery occlusion following major surgical procedures is difficult primarily because of the infrequency of pain as a primary clinical manifestation. In addition, the symptom complex of myocardial infarction postoperatively must be differentiated from surgical and hemorrhagic shock, pulmonary embolism, pulmonary edema, abdominal crises, and other postoperative complications. The more frequent use of the electrocardiograph in the elucidation of unexplained postoperative syndromes will make the diagnosis of coronary occlusion following surgery more readily apparent. During the postoperative period, the classical clinical picture of coronary occlusion with myocardial infarction cannot be relied upon. The therapeutic management of the patient with myocardial infarction due to coronary occlusion following a major operation is essentially no different from that of uncomplicated acute coronary artery occlusions, with the exception that the postoperative surgical management may conflict at times with the medical regimen. The use of anticoagulants is seldom contraindicated in the postoperative patient and should be employed with the aid of precise laboratory control. Detailed supervision of hydration, electrolyte balance, hematological status, and other postoperative surgical problems must be maintained during the therapeutic handling of the medical regimen required in the management of the myocardial infarction.

SUMMARY AND CONCLUSIONS

In the preoperative evaluation it was noted that six patients had minimal signs and symptoms of heart disease with five classified IIB or less and only one as IIIC. Eight could be classified as having only potential heart disease. The electrocardiograms were within complete normal limits in five instances and showed minor abnormalities in three, moderate in seven, and evidence of healed infarction in two patients. Of the four patients called good operative risks one died, and of the three interpreted as poor risks one died.

Anemia and the type of anesthesia did not appear to play a role in the development of postoperative myocardial infarction. Neither did the administration of parenteral fluids or blood appear to be correlated with the onset of this complication.

Significant hypotension developed in seven patients during surgery, and persistent auricular fibrillation developed in one. The duration of the operation failed to show correlation with survival.

During the postoperative period, the course was completely uncomplicated in six patients prior to the onset of infarction. Persistent hypotension in three patients and arrhythmia in two may have been precipitating factors.

The absence of precordial pain is notable, occurring in only 4 (27%) of the 15 patients. Clinical evidence of infarction in the remainder was manifested by persistent hypotension in four, respiratory distress in one, and arrythmia in two. In two additional patients sudden death occurred.

The onset of the infarction occurred within three days postoperatively in 60% of the patients. Forty per cent of the patients succumbed to the myocardial infarction; none of the six patients died who were given anticoagulant therapy.

10. Master, A. M.; Dack, S., and Jaffe, H. L.: Postoperative Coronary Artery Occlusion, J. A. M. A. **110**: 1415-1418 (April 30) 1938.

11. De Santo, D. A.: Operation and Trauma as a Cause of Coronary and Cerebral Thrombosis, Am. J. Surg. **26**: 35-42, 1934. Hamburger, W. W.: The Differential Diagnosis of Cardiac and Gastro-intestinal Lesions, with Particular Reference to Pectoral and Extrapectoral Angina: Angina Pectoris Simulating Gall-Stone Colic, M. Clin. North America **3**: 1677, 1920. Menard, O. J., and Hurxthal, L. M.: Painless Coronary Thrombosis as a Postoperative Complication, S. Clin. North America **11**: 395-401, 1931.

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14. Davis, H. A.; Parlante, V. J., and Hallsted, A. M.: Coronary Thrombosis and Insufficiency Resulting from Shock: Clinical and Pathologic Study, A. M. A. Arch. Surg. **62**: 698-704 (May) 1951.

15. Opdyke, D. F., and Foreman, R. C.: A Study of Coronary Flow Under Conditions of Hemorrhagic Hypotension and Shock, Am. J. Physiol. **148**: 726-739, 1947.

Coronary occlusion with myocardial infarction as a postoperative complication of major surgery cannot readily be anticipated clinically; however, it should be considered in any patient suspected or known to have coronary artery disease and who is to be subjected to a major surgical precedure.

Patients with healed myocardial infarction who are subjected to major surgery are more likely to have fresh infarctions postoperatively than are other patients of the same age group, although the over-all operative mortality increases only moderately.[16] Two of the patients herein reported had a preoperative history and electrocardiographic evidence of healed myocardial infarction.

Coronary artery occlusion can possibly be prevented if surgical or hemorrhagic shock is avoided, anoxia prevented, operative time minimized, noncardiovascular complications prevented or controlled, and if detailed attention is directed toward all other preoperative and postoperative details. When it occurs, postoperatively, myocardial infarction should be diagnosed as early as possible and medical management instituted immediately.

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16. Hannigan, C. A.; Wróblewski, F.; Lewis, W. H., Jr., and LaDue, J. S.: Major Surgery in Patients with Healed Myocardial Infarction, Am. J. M. Sc. **222**: 628-639, 1951. Pfeiffer, P. H., and LaDue, J. S.: Major Surgical Operations in the Presence of Bundle Branch Block: Study of Operative Risk in 59 Patients, ibid. **217**: 369-378, 1949.

AURICULAR THROMBOSIS, MITRAL COMMISSUROTOMY, AND AORTIC EMBOLECTOMY

REPORT OF A CASE

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Perry Blumberg, M.D.
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It is generally accepted that inflammation of the walls of the heart, the small excursion of the auricular muscle, auricular fibrillation, and stasis are the major factors in the production of auricular thrombosis associated with mitral stenosis. Many investigators have reported the incidence of intracardiac thrombosis in rheumatic heart disease.[1] Jordan and co-workers,[2] reviewing 32 cases of mitral stenosis with systemic arterial emboli studied post mortem, found that the number of cases of left auricular appendage thrombosis alone (13 cases) was equaled by the number of cases in which clots occurred in the left atrial chamber alone (5 cases) plus the number of cases in which clots were found in the atrium and appendage simultaneously (8 cases).

From the Surgical Division, Montefiore Hospital.

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2. Jordan, R. A.; Schiefly, C. H., and Edwards, J. E.: Mural Thrombosis and Arterial Embolism in Mitral Stenosis: A Clinicopathologic Study of 51 Cases, Circulation **3**: 363 (March) 1951.

Daley and his co-workers [3] reported that thrombi were found as frequently in the left auricle as in the appendage in 39 cases of rheumatic heart disease studied post mortem. On the basis of their autopsy findings, Daley and co-workers pointed out that auricular appendectomy alone has only a 50% chance of removing the source of the emboli. Hellerstein and associates [4] in 1947 and Burdette [5] in 1949 offered experimental proof of the feasibility of unilateral and bilateral auricular appendage resection in dogs.

Until Madden's [6] report in 1949, the major surgical attack had been leveled at peripheral arterial embolization. Madden reported two cases of resection of the left auricular appendage for recurrent arterial emboli. Baronofsky [7] and Longmire [8] have since reported three cases each (see the accompanying table).

The following case presented many unusual features, one of which concerned the treatment of auricular thrombosis. From the latter standpoint, this case illustrates the necessity of complete exploration of the main chamber of the auricle as well as its appendage.

REPORT OF A CASE

M. N. F., a 42-year-old white married housewife, was admitted on July 26, 1951. Her father had died of coronary artery disease. She had had scarlet fever at the age of 6 years, followed by a bout of rheumatic fever. At 13 her tonsils and adenoids were removed. She had had recurring bouts of pneumonia, at the ages of 17, 19, 34, 38, 39, and 40. A cardiac murmur, which she was told was due to mitral stenosis, had been present since childhood. During her early thirties she was aware of dyspnea on slight exertion on many occasions. At the age of 34 she had severe pneumonia; she then had recurring mild congestive failure for the next four years, requiring digitalis constantly and mercurials intermittently. During this period there was frequent evidence of smoldering rheumatic activity (arthralgias, fever, chest pain, elevated sedimentation rate, lassitude, and easy fatigability). In December, 1950, there was an acute episode resulting in right-sided muscular weakness, involving mainly the right leg and blurring of speech and confusion. There was moderate recovery from the residuum, but between December, 1950, and July, 1951, there were five further episodes, each increasing in severity and involving eventually the right arm and right side of the face as well. On July 14, 1951, occurred the severest attack, resulting in unconsciousness, shock, and paralysis of the right half of the body with a Jacksonian type of convulsion involving the right arm. Treatment of the shock and administration of papaverine brought some measure of improvement. The patient had been receiving digoxin, 0.25 mg. daily. Physical examination revealed the following pertinent findings. There was right hemiparesis with involvement of the right side of the face and associated dysarthria. The heart rhythm was totally irregular. A rough grade 2 diastolic murmur with presystolic accentuation and a short, rough grade 2 systolic murmur were heard in the apical area in a small radius, with some radiation toward the sternum. A short diastolic thrill was felt in the same area. The second pulmonic sound was louder than the second aortic sound. The blood pressure was 110/68 mm. Hg. The liver and spleen were not palpable. There was no engorgement of the neck veins or peripheral edema. Fluoroscopy and roentgenograms of the chest revealed moderate enlargement of the left auricle and slight enlargement of the right ventricle. The other chambers showed no enlargement. There was a faint stippling of the lung fields with accentuation of the bronchopulmonary markings at both hilar areas. The electrocardiogram was interpreted as revealing right axis deviation and auricular fibrillation. There was no electrocardiographic evidence of left ventricular hypertrophy. The RS-T changes were those commonly seen with digitalis administration (an electrocardiogram in 1946 had demonstrated regular sinus rhythm with broad notched P_{3-5} and digitalis effects). Other laboratory studies were within normal limits. Because of the repeated almost identical patterns

of the cerebral attacks, the question of brain tumor or intrinsic arterial disease was discussed. Lumbar puncture studies revealed normal hydrodynamics and normal chemical composition. A neurological consultant expressed the opinion that cardiac exploration was not contraindicated.

Accordingly, we decided to explore the left auricle, remove the mother thrombus, and perform commissurotomy to combat the factor of stasis in the production of further thrombosis.

Operation.—On July 30, 1951, the patient was anesthetized with a mixture of cyclopropane, ether, and oxygen with an endotracheal tube in place. With the patient in the left lateral position the chest was opened through the fourth intercostal space. The lung was normal to palpation. The pericardium was thin and seemed to contain a normal amount of clear serous fluid. When the pericardium was opened, a few premature ventricular contractions were observed on the monitoring electrocardiogram. The left auricular appendage was hypertrophied but contained no palpable thrombus. Double purse-string sutures were placed at the base and a clamp above these. The tip of the auricular appendage was excised. A finger was inserted into the left auricle. Immediately a soft nubbin-like mass was felt nudging softly against the tip of the exploring finger. The purse-string suture around the finger was loosened and the finger partially withdrawn. A gush of blood was expelled from the appendage, and the thrombus could no longer be felt. The purse-string suture was tightened about the finger and exploration of the auricle continued. No other thrombi were felt. No interauricular septal defect was present. The mitral valve was a thin structure with a firm fibrous oval ring at the ostium, approximately 1 by 0.3 cm. in size. The valve leaflets were flexible. Commissurotomy was readily performed by finger fracture of the anterolateral commissure. The resulting orifice readily admitted two fingers, the size now being at least 2.5 cm. in the long diameter. A faint regurgitant thrill became palpable. During cardiac exploration the electrocardiogram showed some ventricular premature contractions followed by a short period of ventricular tachycardia during the actual commissurotomy. A few more ventricular premature contractions were observed while the finger was being removed. The heart then resumed its preoperative rhythm of auricular fibrillation. The purse-string sutures were tied and the margins of the auricular appendage oversewn. This effectively obliterated the chamber of the appendage. The pericardium was loosely approximated with interrupted sutures. The tip of the lingula of the left upper lobe was excised for histological study of the pulmonary arterioles. Pleural drainage was accomplished by an intercostal stab wound in the sixth interspace in the posterior axillary line. The ribs were approximated with interrupted pericostal sutures, and the chest wall was closed in layers. During the procedure about 300 cc. of whole blood was infused, most of it at the time of ejection of blood from the auricle. The patient's blood pressure dropped slightly during the procedure but was at its preoperative level at the close. The patient's general condition seemed good. The operation was begun at 9:30 a. m. and terminated at 11:30 a. m.

By noon it became apparent that the thrombus had not been expelled during the gush of blood at operation. The femoral pulses were absent. Both legs were cold, and marbleization of the skin was in evidence, the left leg appearing more involved than the right. Oscillometric readings were totally absent. The patient's condition was deteriorating rapidly. The blood pressure fell, reaching a level of 38/10. A transfusion was started, and at 2:35 p. m., three hours after the close of the first operation, the patient was reanesthetized with ethylene, ether, and oxygen. The preoperative diagnosis was saddle embolus of the aorta.

A left paramedian suprapubic incision was performed. Numerous adhesions between the bowel and the anterior abdominal wall were present. These were freed by sharp dissection. The small bowel was eviscerated. Pulsations were present above the bifurcation of the aorta and absent below it. A thrombus was felt at the bifurcation and extending proximally for a distance of 2 cm. The head of the thrombus was felt in the right iliac artery. The head of the thrombus in the left iliac artery could not be palpated. An incision was made through the peritoneum over the left iliac artery. The artery was isolated with umbilical tapes. An incision was made into the artery, which was found to be filled with an old organized clot. The right iliac artery was then isolated and incised. A fresh clot immediately extruded from the wound. Suction and milking yielded more clot, with disappearance of the mass at the bifurcation. Distal suction in the right iliac and femoral failed to yield further clot, and brisk bleeding occurred from above and below. The old clot in the left iliac artery was cleaned out and as much intima as possible excised. After suction, brisk bleeding occurred from the aortic and distal segment of the artery. The arterial wounds were closed, with continuous sutures, with an everting suture used on the right side. Forty milligrams of heparin was injected into the aorta at its bifurcation. An attempt was made to isolate the right sympathetic chain, but brisk bleeding was encountered when the inferior vena cava was mobilized. This was controlled by clamp and an absorbable hemostatic (oxycel®). Procaine hydrochloride was injected into the area of the right lumbar sympathetic chain. The peritoneum was sutured over the arteries with

Collected Cases of Auricular Appendectomy

Surgeon	Pathological Findings	Operation	Complication	Result
Madden	Chronic rheumatic heart disease; mitral stenosis; auricular fibrillation	Left auricular appendectomy	Immediate postoperative hemiparesis	No further emboli for 8 mo.
Madden	Chronic rheumatic heart disease; mitral stenosis; auricular fibrillation	Left auricular appendectomy	.....	Died 4 days postoperatively; no autopsy
Baronofsky	Mitral lesion; auricular fibrillation	Left auricular appendectomy	.....	Remained well
Baronofsky	Chronic rheumatic heart disease; mitral stenosis; auricular fibrillation	Left auricular appendage ligation	.....	Remained well
Baronofsky	Mitral stenosis; auricular fibrillation	Left auricular appendage ligation	.....	Died 2 mo. postoperatively with continued gastrointestinal bleeding
Longmire	Mitralization of heart; auricular fibrillation	Left auricular appendectomy	Required bilateral midthigh amputation 15 days postoperatively	No further embolization
Longmire	Mitral stenosis; auricular fibrillation	Right auricular appendectomy	.....	Remained well
Longmire	Chronic rheumatic heart disease; auricular fibrillation	Left auricular appendectomy	.....	Remained well

3. Daley, R., and others: Systemic Arterial Embolism in Rheumatic Heart Disease, Am. Heart J. **42**: 566 (Oct.) 1951.

4. Hellerstein, H. K.; Sinaiko, E. S., and Dolgin, M.: Amputation of Canine Atrial Appendages, Proc. Soc. Exper. Biol. & Med. **66**: 337 (Nov.) 1947.

5. Burdette, W. J.: Removal of Auricular Appendage in the Dog, Surg., Gynec. & Obst. **89**: 623 (Nov.) 1949.

6. Madden, J. L.: Resection of Left Auricular Appendix: A Prophylaxis for Recurrent Arterial Emboli, J. A. M. A. **140**: 769 (July 2) 1949.

7. Baronofsky, I. D., and Skinner, A.: Ligation of Left Auricular Appendage for Recurrent Embolization, Surgery **27**: 848 (June) 1950.

8. Longmire, W. P., Jr.; Beal, J. M., and Leake, W. H.: Resection of Auricular Appendages, Dis. Chest **19**: 307 (March) 1951.

interrupted sutures. The abdominal wall was closed in layers without drainage. The patient was returned to the recovery room in fair condition. The blood pressure at this time was 116/82. Microscopic examination of the excised auricular muscles revealed hypertrophy of the auricular fibers only. The pulmonary parenchyma was within normal limits.

On the night of the operating day, the patient's condition was fair. Blood pressure was maintained at 120/80. The legs were warm, with the right warmer than the left. A right femoral pulsation was present.

The patient's general condition continued good the first postoperative day, although there was difficulty in cough and expectoration, owing to the hemiparesis. In the afternoon, however, the legs became cooler; the femoral pulsation on the right became perceptibly weaker and was absent according to some observers. A continuous caudal plastic catheter was inserted, and 20 cc. of 1% procaine plus 2 cc. of 0.5% tetracaine (pontocaine®) hydrochloride was instilled. The patient's systolic blood pressure immediately dropped to 80. Five milligrams of methamphetamine hydrochloride was injected intravenously, with an immediate response of the systolic pressure to 115 mm. Hg. Ten milligrams of methamphetamine was then given intramuscularly. The right femoral pulsation again became apparent. It was realized at this time that heparinization had not been carried out according to plan. This patient was therefore reheparinized intravenously to maintain the clotting time at 25 to 30 minutes.

On the second day, the patient's general condition was fair. The left lung seemed completely reexpanded (confirmed by roentgenogram). However, a few tracheobronchial rales were heard throughout and some crepitant rales were heard at right base posteriorly. A minimal amount of subcutaneous emphysema was felt over the left side of the thorax. However, the urinary output was only 180 cc. postoperatively, in spite of liquid intake of about 3,500 cc. during the two previous days. An indwelling catheter was then placed in the urinary bladder. It was felt that the oliguria was due to hypotension, decreased glomerular filtration, and dehydration. The laboratory findings of normal sodium potassium and chlorides with a urea rise to only 24.5 mg. and no red blood cells in the urine seemed to substantiate the cause of the oliguria.

On the third day, the subcutaneous emphysema continued to increase, in spite of a completely reexpanded left lung. The wound was inspected. No herniation of lung was apparent. There was considerable production of mucus, and roentgenogram of the chest revealed atelectasis of the right lower segments. Bronchoscopy was attempted. The patient's pharynx was anesthetized with 20% cocaine. The left upper and lower eyelids became edematous, and the patient appeared to go into shock. Secobarbital (seconal®) sodium, 50 mg. was administered intravenously and the bronchoscopy performed. Considerable mucus and a firm mucous plug were aspirated from the lower lobe of the right lung. Breath sounds following bronchoscopy became clearer and respirations slower and easier.

On the fourth day, the subcutaneous emphysema persisted. Inspection of the wound revealed a raised area over the sternal aspect of the wound, which seemed to contain air. This was approached with a needle, and air was freely obtained without change in the character of the swelling. Breath sounds over this area were bronchial in character and were closer to the ear than elsewhere. It was felt that herniation of lung with necrosis had occurred. A pressure dressing was applied. The subcutaneous emphysema hereafter was redistributed over the neck and face but did not increase; shortly thereafter it began to subside. The urinary output was 200 cc. The patient's general condition improved slowly, although the urinary output remained low. Intravenously heparin therapy was continued.

On the sixth day, gross hematuria was noted. The clotting time was six minutes. The indwelling catheter was removed and heparin therapy discontinued. From this point on the improvement was more apparent. The urinary output was good. By the seventh postoperative day the blood urea nitrogen was 8 mg. per 100 cc. The subcutaneous emphysema subsided. The patient's speech improved. The wounds healed by first intention.

Physical therapy was begun, and the patient made marked improvement in speech, ability to use her hand, and to walk. She was kept in the hospital longer than was necessary, owing to home factors. On discharge, Sept. 9, no murmurs were heard over the cardiac area. The right femoral pulsation was felt. Both legs were in good condition.

COMMENT

The above case represents, we believe, the first reported attempt to remove a thrombus confined to the main left auricular chamber. Certain cardiac surgeons are reported to incise the auricular appendage and to permit free bleeding before inserting the finger, hoping thereby to expel a possible auricular clot. It may be that such a procedure would have been successful in this case. One of us (A. E. B.) is at present engaged in designing an instrument that we hope will safeguard the orifice of the mitral valve during thrombectomy. The presence of an old clot in the left iliac artery sustained us in the belief that the auricular clot was the source of the cerebral emboli. Whether the occlusive symptoms produced in the left extremity were all due to arterial spasm or whether the clot occluded a recanalized channel in the old thrombus cannot be determined. Of extreme interest is the fact that after the saddle embolus and the failure to palpate both femoral arteries, no one could recall having palpated these vessels preoperatively. Had we known that the left iliac artery was occluded preoperatively, we might not have done a transabdominal procedure. From the pathological changes observed, however, it is felt that the transperitoneal approach gave more satisfactory results than one might have obtained with the right femoral approach. The patient was thus subjected to general anesthesia a second time, however.

The collapse of the peripheral vascular system after a caudal anesthesia and its prompt recovery with methamphetamine hydrochloride therapy is worthy of note. While there is no positive proof that herniation and incarceration of the lung through the intercostal incision occurred, the physical findings and the subsequent course strongly support the possibility. It is impossible, of course, to know whether the portion of the lung that became incarcerated and necrotic, with the development of a bronchosubcutaneous fistula, was the lingular tip that had been subjected to biopsy or another portion. In our experience this has been a unique complication.

The hematuria that occurred on the sixth day at first glance may have been caused by any one of three factors. The indwelling catheter may have produced localized hemorrhagic cystitis; an embolus to the kidney may have occurred; finally, the bleeding may have been a response to heparin therapy, although the coagulation time was not markedly prolonged. The prompt disappearance of the hematuria and the subsequent profuse diuresis seem to indict the catheter as the inciting factor.

As regards the role of anticoagulant therapy, Askey and Cherry [9] followed 20 patients, after the establishment of arrhythmias, with continuous anticoagulant treatment. In 4 of the 20, thromboembolism occurred after bishydroxycoumarin (dicumarol®) therapy had been started. In only 11 were the results classified as excellent, and 7 of these had not had previous embolic

9. Askey, J. M., and Cherry, C. B.: Thromboembolism Associated with Auricular Fibrillation, Continuous Anticoagulant Therapy, J. A. M. A. **144**: 97 (Sept. 9) 1950.

phenomena. Fourteen patients were readily controlled with anticoagulant therapy while ambulatory; six were difficult to control. Soulie, Chichie, and Papanicolis [10] were opposed to the prophylactic administration of anticoagulants because of difficulty in case selection and the fact that clots are found post mortem despite adequate and prolonged anticoagulant therapy. There are numerous reports of embolization occurring during anticoagulant therapy.[11] It is our feeling that anticoagulant therapy may prevent further clot formation but will not prevent embolization from an established mother thrombus.

Finally, the importance of performing commissurotomy at the time of thrombectomy is stressed. Briggs, in a discussion of Longmire's [8] paper, stated that Baronofsky had mentioned this measure to him. It may be that the prevention of stagnation of blood in the left auricle behind a stenotic valve is the most important factor in the prevention of thrombus formation in the left auricle or its appendage.

SUMMARY

The details of treatment of a patient with rheumatic heart disease, mitral stenosis, auricular fibrillation, and multiple embolic phenomena are presented. Emphasis is placed on left atrial as well as appendiceal exploration. The necessity for mitral commissurotomy at the time of exploration is stressed.

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10. Soulie, P.; Chichie, P., and Papanicolis, I.: Les thromboses pariétales organisées des cavités du coeur, Arch. d. mal. du coeur **42**: 669 (July) 1949.

11. Profitt, J. H.; Yarborough, J. A.; Auerbach, S. H., and McCleery, R. S.: Left Auricular Appendage Thrombosis with Aortic and Multiple Arterial Emboli: Case Report, Ann. Surg. **133**: 109 (Jan.) 1951.

COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

POLYMYXIN

Polymyxin is the generic term employed to designate a series of related antibiotics derived from various strains of the spore-forming soil bacterium, Bacillus polymyxa (B. aerosporus Greer). The various polymyxins which have been isolated are differentiated by affixing letters of the alphabet which do not necessarily signify the order of isolation: polymyxin A, polymyxin B, etc. Polymyxin B, is the least toxic of those adequately studied. Chemically, the polymyxins are basic polypeptides. Polymyxin B contains leucine, threonine, phenylalanine, α,γ-diaminobutyric acid and a fatty acid of empirical formula, $C_9H_{18}O_2$, and has a molecular weight of about 1,000. It is stable as the acid salt, polymyxin B sulfate, in the dry state; in solution it is stable for extended periods if buffers are added. Alkaline solutions are less stable. The antibiotic is highly effective in vitro against many gram-negative micro-organisms. See the monograph on polymyxin B sulfate

Polymyxin B Sulfate.—Aerosporin Sulfate (Burroughs Wellcome).—A basic polypeptide containing leucine, threonine, phenylalanine, α,γ-diaminobutyric acid and a fatty acid of unknown structure (empirical formula, $C_9H_{18}O_2$).

Actions and Uses.—Polymyxin B sulfate, an antibiotic derived from an isolated strain of Bacillus polymyxa, is bactericidal in vitro for most gram-negative micro-organisms. Escherichia coli, Shigella, Pseudomonas aeruginosa (B. pyocyaneus), Aerobacter aerogenes, Klebsiella pneumoniae and Hemophilus influenzae are sensitive to Polymyxin B sulfate concentrates of 0.05 to 2 μg. per cubic centimeter. Proteus vulgaris (B. proteus) is usually more resistant. Most strains of P. aeruginosa are highly sensitive. Clinical observations indicate that the development of bacterial resistance is unlikely.

Polymyxin B sulfate is effective clinically by intramuscular injection (and intrathecally, when indicated) for the treatment of pseudomonal (pyocyaneal) bacteremia, meningitis and urinary tract infection, and for the treatment of meningitis caused by other gram-negative bacilli such as Aerobacter aerogenes, E. coli, K. pneumoniae, and H. influenzae when these are more sensitive to polymyxin B than to other effective antibiotics. Since the antibiotic does not readily pass into the spinal fluid when given intramuscularly, the drug should be given intrathecally as well as intramuscularly for the treatment of susceptible meningeal infections. The intrathecal doses required do not produce systemic toxic effects and the drug is considered relatively nonirritating to the meninges. Intrathecal injections should be made with the care that is essential in the performance of repeated spinal punctures.

Polymyxin B sulfate, when given parenterally, may produce neurotoxic and/or nephrotoxic effects, but it has a low degree of toxicity when used in doses below 3 mg. per kilogram of body weight. Neurologic disturbances are usually subjective and include dizziness, mild weakness, and paresthesias of the mouth, face, and less frequently, of the extremities. These are not usually considered sufficiently serious to warrant discontinuance of therapy. Nephrotoxic effects, with damage to the kidney tubular epithelium, are manifested by albuminuria and nitrogen retention. The danger of renal damage is minimal when the drug is administered within the recommended dosage range. Other toxic effects include occasional drug fever, and pain at the site of injection which can be lessened by employing 1% procaine hydrochloride solution in the diluent. The possible danger of renal damage makes it desirable to limit the parenteral use of the drug to patients who are under close observation, where there is access to adequate laboratory facilities. Renal dysfunction and nitrogen retention do not contraindicate injection of the drug when it is specifically indicated unless such use is found to aggravate preexisting renal damage.

Polymyxin B sulfate is aslo useful by topical application for systemic treatment of certain intestinal infections such as Shigella or Pseudomonas enteritis, when present as a pathogen. It is too poorly absorbed orally to warrant use by this route in the treatment of systemic infections. Toxic manifestations have not been observed with oral use of the drug.

Polymyxin B Sulfate is also useful by topical application for the treatment of local infections caused by susceptible gram-negative bacilli, especially Pseudomonas aeruginosa. It may be employed locally also to prevent contamination by gram-negative organisms of wounds or burns.

Dosage.—Intramuscularly, the average daily dosage extends from 1.5 mg. (15,000 units) to 2.5 mg. (25,000 units) per kilogram of body weight. The total daily dosage should not exceed 2.5 mg. per kilogram and, in any case, not more than 0.2 gm. (2 million units). The drug is usually administered in three divided doses at six- to eight-hour intervals. Such doses provide therapeutic blood serum levels of 1 to 8 μg. per cubic centimeter. The peak level is reached within 30 minutes to two hours after injection; one-half the peak level is present after six hours, with detectable levels up to 12 hours' duration. In patients with impaired renal function and nitrogen retention, a dosage of 20 mg. every eight hours maintains serum levels at 2.5 μg. per cubic centimeter. A solution for intramuscular use is prepared by dissolving 50 mg. in water for injection-U. S. P., sterile isotonic sodium chloride solution, or 0.5 cc. of 1% sterile procaine hydrochloride solution. If procaine is used, the usual precaution should be observed.

Intrathecally, the following doses are suggested: Children under two years of age, 2 mg. daily for three or four days, then 2.5 mg. every other day; children over two years and adults, 5 mg. daily for three or four days, then 5 mg. every other day. A solution for intrathecal injection is prepared by adding 10 cc. of sterile isotonic sodium chloride solution to 50 mg. of the drug. Solutions prepared for intramuscular use and containing procaine should not be used for intrathecal administration.

Orally, for adults and older children, the dosage is 75 to 100 mg. four times daily; children two to five years of age, 50 to 75 mg. three times daily; children up to two years of age, 25 to 50 mg. three times daily. For infants and young children the tablets may be crushed and mixed with a suitable food or dissolved in water and flavored as desired.

For topical application, the drug, in sterile dry form, is dissolved in distilled water or isotonic sodium chloride solution for administration as drops, spray, wet dressing or irrigation. Concentrations of 0.1% (10,000 units per cubic centimeter) to 0.25% (250,000 units per cubic centimeter) are considered to be effective and nonirritating. Concentrations of 1% or more may produce local irritation when applied to sensitive areas such as the eye. Neither bacterial resistance nor sensitivity reactions have been observed, but until further experience is gained, a total of not more than 2 billion units daily should be applied in cases of severe burns and open wounds. Solutions of the antibiotic are stable for at least six months if kept under refrigeration.

Tests and Standards.—

Physical Properties: Polymyxin B sulfate is a white to cream-colored irregular scale-like material, which has no definite melting point, but decomposes at about 230°. It is soluble in water and isotonic sodium chloride solution. A 2% solution has a pH of about 5.7.

Identity Tests: Dissolve about 10 mg. of polymyxin B sulfate in 50 ml. of water. On 5 ml. portions of this solution perform the following identity and purity tests. To one portion in a test tube add 0.5 ml. of 0.1% ninhydrin and 2 drops of pyridine, boil for 1 min. and cool: a blue color develops *(presence of α-amino acid)*. To a second portion of polymyxin B sulfate solution in a test tube, add 5 ml. of 10% sodium hydroxide and mix thoroughly. Add 0.5% copper sulfate dropwise, mixing between drops: a pinkish-violet color is produced *(presence of peptone or proteose)*.

Purity Tests: To 5 ml. of the 0.02% solution of polymyxin B sulfate prepared as directed in the identity tests, add 0.5-1 ml. of 0.1% α-naphthol in 0.5% sodium hydroxide. Add 1% sodium hypochlorite dropwise avoiding an excess: no transitory red color appears *(absence of free protein)*.

Dry a sample of polymyxin B sulfate at 37° for 4 hours in a vacuum oven at 5 mm. or less: the loss in weight is not greater than 4.0%.

To about 0.1 Gm. of polymyxin B sulfate in a platinum dish add 4 ml. of sulfuric acid and heat cautiously over a low flame until fumes no longer evolve. Ignite the residue in a muffle furnace: the amount of sulfated ash is not greater than 5.0%.

Assay: Polymyxin B sulfate is assayed microbiologically according to the requirements of the Food and Drug Administration.

Dosage Forms of Polymyxin B Sulfate

POWDER. The powder responds to the tests described in the section on active ingredient in the monograph for polymyxin B sulfate.

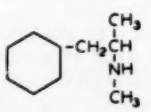
TABLETS. *Assay:* Polymyxin B sulfate tablets are assayed microbiologically according to the requirements of the Food and Drug Administration.

Burroughs Wellcome & Company, Inc., Tuckahoe, New York

Aerosporin Sulfate (Parenteral): 500,000 unit vials.

Tabloids Aerosporin Sulfate: 500,000 units. U. S. Patent 2,565,057. U. S. Trademark 505,252.

Propylhexedrine.—Benzedrex (Smith, Kline & French).—$C_{10}H_{21}N$.—M.W. 155.28.—N,α-Dimethylcyclohexaneëthylamine.—The structural formula of propylhexedrine may be represented as follows:



Actions and Uses.—Propylhexedrine is closely related to, and shares the actions and uses of, amphetamine and similar volatile sympathomimetic amine compounds. It produces vasoconstriction and a decongestant effect on the nasal mucous membranes. Propylhexedrine has only about one-half the pressor effect of amphetamine and produces decidedly less effect on the central nervous system. Propylhexedrine therefore is useful primarily for its local shrinking effect upon the nasal mucosa in the symptomatic relief of nasal congestion caused by the common cold, allergic rhinitis, or sinusitis. Its volatility makes propylhexedrine convenient for intranasal application by inhalation and for reaching structures sometimes inaccessible to liquid forms of medication. Because of its wide margin of safety and relative freedom from toxic side-effects, the use of propylhexedrine by inhalation is not contraindicated for patients in whom an ephedrine-like action would be undesirable. It is considered safe for self-medication by adults, but children should not have unsupervised access to an inhaler.

Dosage.—Propylhexedrine is administered by nasal inhalation with a portable inhaler containing 0.25 gm. of the drug. The inhaler should be kept closed tightly between applications to avoid loss of the volatile contents. The usual dose is two inhalations through each nostril (about 0.5 mg.). This dose may be repeated as required to obtain relief. When the inhaler is cold, it should be warmed in the hand before use because the volatility of propylhexedrine is reduced by cooling. With ordinary use, a 0.25 gm. container will retain its effectiveness two to three months.

Tests and Standards.—

Physical Properties: Propylhexedrine is a clear, colorless liquid with a characteristic amine odor, b.p. 202-206°. Propylhexedrine is very slightly soluble in water; and soluble in dilute acids, alcohol, and ether.

Identity Tests: To about 0.1 gm. of propylhexedrine suspended in 5 ml. of water add 3-5 ml. of mercuric chloride T.S.: a copious white, granular precipitate forms *(distinction from epinephrine, ephedrine, and phenylephrine)*.

To a water suspension of about 0.1 gm. of propylhexedrine add 2 ml. of iodine T.S.: a brown precipitate forms.

To about 0.1 gm. of propylhexedrine suspended in 5 ml. of water add 5 ml. of saturated picric acid solution. The oily precipitate slowly crystallizes. Filter the mixture and dry the precipitate in an Abderhalden pistol dryer at 56-57° for about 4 hours: the picrate melts at 108-110°.

Purity Tests: Ash about 0.5 gm. of propylhexedrine, accurately weighed: the residue does not exceed 0.1%.

Assay: Accurately weigh about 0.5 gm. of propylhexedrine, transfer it to a 250 ml. Erlenmeyer flask by rinsing the container with 10-20 ml. of neutral alcohol, add 50 ml. of neutral alcohol to the solution, and titrate with 0.1 *N* sulfuric acid, using methyl red T.S. as an indicator. Each milliliter of 0.1 *N* acid is equivalent to 0.01553 gm. of propylhexedrine. The amount of propylhexedrine is not less than 98.0 nor more than 102.0%.

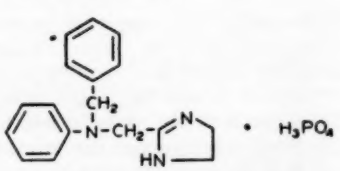
Dosage Forms of Propylhexedrine

INHALER. *Assay:* (Propylhexedrine) Place the pledgets from 3 inhalers in a Soxhlet extraction thimble of suitable size. Quickly assemble the Soxhlet apparatus. Rinse the pledget containers with 10-20 ml. of neutral alcohol and pour the rinsings into the extraction flask through the condenser. Extract the pledgets for a minimum of 20 cycles with about 50 ml. of neutral alcohol. Cool the extract and titrate it with 0.1 *N* sulfuric acid, using methyl red T.S. as an indicator. Each milliliter of 0.1 *N* acid is equivalent to 0.01553 gm. of propylhexedrine. The amount of propylhexedrine is not less than 98.0% of the labeled amount.

Smith, Kline & French Laboratories, Philadelphia.

Inhaler Benzedrex: Each inhaler contains 0.25 gm. of propylhexedrine. U. S. Patent 2,454,746. U. S. Trademark 438,149 and 438,148.

Antazoline Phosphate.—Antistine Phosphate (Ciba).—$C_{17}H_{19}N_3 \cdot H_3PO_4$.—M.W. 363.35.—2-(N-Benzylanilinomethyl)-2-imidazoline phosphate.—The structural formula of antazoline phosphate may be represented as follows:



Actions and Uses.—Antazoline phosphate shares the action of its hydrochloride salt and other antihistamine compounds. See the general statement on Histamine-Antagonizing Agents and the monograph on Antazoline Hydrochloride. The phosphate is preferable to the hydrochloride for ophthalmic application in the management of ocular allergies because it produces less smarting and stinging. Systemic therapy by oral administration of antazoline hydrochloride is sometimes desirable to supplement local treatment in the eye.

Dosage.—An 0.5% isotonic solution of antazoline phosphate is employed for instillation in the eye. One or two drops are instilled in each eye every three or four hours or less frequently as required to relieve symptoms.

Tests and Standards.—

Physical Properties: Antazoline phosphate is a white, odorless, crystalline powder with a bitter taste. It melts with decomposition between 194 and 198°. It is soluble in water, sparingly soluble in methanol, and practically insoluble in benzene and ether. The pH of a 2% solution is about 4.5.

Identity Tests: Dissolve about 0.2 gm. of antazoline phosphate in 20 ml. of water. To 2 ml. of this solution add 5 drops of ammonium reineckate T.S.: a flocculent pink precipitate forms. To 5 ml. of the solution slowly add 5 ml. of picric acid T.S.: a yellow precipitate forms which melts between 155 and 159°. To 2 ml. of the solution add 10 drops of nitric acid: the solution turns red and then immediately turns dark green. To 2 ml. of the solution add a few drops of ammonium molybdate T.S.: a yellow precipitate forms which is soluble in diluted nitric acid or ammonia T.S. *(presence of phosphate).* To 5 ml. of the solution add enough 5% sodium hydroxide to make it distinctly alkaline: the free base which precipitates melts between 114 and 118°.

A 0.001% solution, prepared as directed later in the spectrophotometric assay for antazoline phosphate, exhibits an ultraviolet absorption maximum at about 2420 Å [specific absorbancy, E(1%, 1 cm.), 414 ± 5].

Purity Tests: Dry about 1 gm. of antazoline phosphate, accurately weighed, for 4 hours at 105°: the loss in weight is not more than 0.5%.

Char about 1 gm. of antazoline phosphate over a low flame. Cool and add 1 ml. of sulfuric acid and continue ignition until no carbon remains: the residue is not more than 0.2%.

Assay: (Antazoline Phosphate) Transfer to a 1000 ml. volumetric flask 0.1 gm. of antazoline phosphate, accurately weighed, and fill to the mark with water. Mix thoroughly, transfer 10 ml. of this solution to a 100 ml. volumetric flask, and fill to the mark with water. Measure the absorbancy of the final solution (0.001%) at 2420 Å, using water as a blank. The concentration of the final solution in mg./ml. = absorbancy ÷ 41.4. The amount of antazoline phosphate present is not less than 97.0 nor more than 103.0%.

(Antazoline) Transfer to a 150 ml. beaker about 0.2 gm of antazoline phosphate, accurately weighed, and add about 25 ml. of water. Slowly, with vigorous stirring, add 50 ml. of picric acid T.S. Allow the mixture to stand for at least 2 hours and transfer the precipitate to a tared sintered glass crucible, using the filtrate to effect complete transfer. Wash the precipitate first with picric acid solution and then with two 2 ml. portions of ether. Dry the precipitate to constant weight (about 4 hours) in a vacuum desiccator over phosphorus pentoxide. Each gram of picrate formed is equivalent to 0.5367 gm. of antazoline and 0.7350 gm. of antazoline phosphate. The amount of antazoline present is not less than 70.8 nor more than 75.2%, equivalent to not less than 97.0 nor more than 103.0% of antazoline phosphate.

Dosage Forms of Antazoline Phosphate

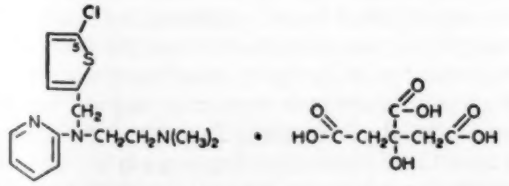
SOLUTION. *Identity Tests:* The solution responds to the identity tests given in the monograph for antazoline phosphate.

Assay: (Antazoline Phosphate) Transfer to a 150 ml. beaker an amount of solution, accurately measured, equivalent to 0.1 gm. of antazoline phosphate. Add slowly, with vigorous stirring, 50 ml. of picric acid T.S. Proceed as directed in the second assay in the monograph for Antazoline Phosphate starting with, "Allow the mixture to stand . . ." Each gram of picrate formed is equivalent to 0.7350 gm. of antazoline phosphate. The amount of antazoline phosphate present is not less than 95.0 nor more than 105.0% of the labeled amount.

Ciba Pharmaceutical Products, Inc., Summit, N. J.

Ophthalmic Solution Antistine Phosphate 0.5%: 15 cc. dropper bottles. A solution containing 5 mg. of antazoline phosphate in each cubic centimeter. Preserved with 0.0065% methylparaben and 0.0035% propylparaben. U. S. Patent 2,449,241. U. S. trademark 432,457.

Chloromethapyrilene Citrate.—Chlorothen Citrate (Whittier).—$C_{13}H_{19}ClN_3S.C_6H_8O_7$.—M.W. 487.96.—2-[(2-Dimethylaminoethyl)-2-(5-chlorothenylamino)]pyridine citrate.—N,N-Dimethyl-N′-(2-pyridyl)-N′-(5-chloro-2-thenyl)ethylenediamine citrate.—The structural formula of chloromethapyrilene citrate may be represented as follows:



Actions and Uses.—See general statement on histamine antagonizing agents.

Dosage.—The average adult dose is 25 mg. administered orally.

Tests and Standards.—

Physical Properties: Chloromethapyrilene citrate is a white, practically odorless solid. It melts between 116 and 118°. It is very slightly soluble in ether. The amounts which dissolve in the following solvents to form 100 ml. of solution are 2.5 gm. in alcohol and 4.7 gm. in water. When sodium hydroxide T.S. is added to a 1% solution, the free base is obtained as an oil. The 1% solution is clear and colorless, and has a pH between 3.9 and 4.1.

Identity Tests: To 0.1 gm. of chloromethapyrilene citrate dissolved in 10 ml. of water add an excess of a saturated solution of picric acid. Allow the mixture to stand for about 1 hour, filter, wash the precipitate with water, and dry at 105°: the dipicrate melts between 150 and 152°.

To 5 ml. of a 1% solution of chloromethapyrilene citrate add 0.5 ml. of mercuric sulfate T.S. and heat to boiling: a precipitate forms. Cool and filter the mixture, and to the clear yellow filtrate add potassium permanganate T.S.: a white precipitate forms *(presence of a citrate).*

A 0.001% solution in alcohol, prepared as directed in the spectrophotometric assay for chloromethapyrilene citrate, exhibits ultraviolet maxima at 2420 Å [specific absorbancy, E(1%, 1 cm.), about 410] and at 3050 Å [specific absorbancy, E(1%, 1 cm.), about 89].

Purity Tests: Dry about 2 gm. of chloromethapyrilene citrate, accurately weighed, over phosphorus pentoxide for 18 hours: the loss in weight does not exceed 0.1%.

Char about 0.5 gm. of chloromethapyrilene citrate, cool the residue, add a few drops of sulfuric acid, and continue ignition until no carbon remains: the amount of residue does not exceed 0.05%.

Assay: (Chloromethapyrilene Citrate) Transfer to a 100 ml. volumetric flask 0.1 gm. of chloromethapyrilene citrate, fill to the mark with alcohol, and mix thoroughly. Transfer 10 ml. of this solution to another 100 ml. volumetric flask, fill to the mark with alcohol, and again mix thoroughly. To a third 100 ml. volumetric flask add 10 ml. of this solution, fill to the mark with alcohol, and mix thoroughly. Determine the absorbancy of the final solution (0.001%) at 2420 Å. The concentration of the final solution in mg./ml. = absorbancy ÷ 41. The amount of chloromethapyrilene citrate present is not less than 98.5 nor more than 101.5%.

(Citrate) To a 250 ml. beaker add 0.3 gm. of chloromethapyrilene citrate, accurately weighed. Dissolve it in 50 ml. of water and titrate electrometrically with 0.1 *N* sodium hydroxide to a pH of 9.6. Each milliliter of 0.1 *N* sodium hydroxide is equivalent to 0.006404 gm. of citrate and 0.01626 gm. of chloromethapyrilene citrate. The amount of citrate present is not less than 38.8 nor more than 40.0%, equivalent to not less than 98.5 nor more than 101.5% of chloromethapyrilene citrate.

(Nitrogen) Transfer to a semimicro Kjeldahl flask about 0.3 gm. of chloromethapyrilene citrate, accurately weighed, and digest it for 4 hours with 7 ml. of sulfuric acid, 2.7 gm. of potassium sulfate and 0.3 gm. of mercuric oxide. Cool the flask, add 15 ml. of water, make the solution alkaline with 40% sodium hydroxide, and then add 10 ml. of 40% sodium thiosulfate. Distil the ammonia into 20 ml. of 4% boric acid. Using a mixed indicator (1:5 methyl red T.S. and bromocresol green T.S.), titrate the liberated ammonia with 0.1 *N* hydrochloric acid. Each milliliter of 0.1 *N* acid is equivalent to 0.001401 gm. of nitrogen and 0.01627 gm. of chloromethapyrilene citrate. The amount of nitrogen present is not less than 8.50 nor more than 8.70% equivalent to not less than 98.5 nor more than 101.5% of chloromethapyrilene citrate.

Dosage Forms of Chloromethapyrilene Citrate

TABLETS. *Identity Tests:* The powdered tablets respond to the identity tests listed in the monograph for chloromethapyrilene citrate.

Assay: (Chloromethapyrilene Citrate) Transfer to a 100 ml. volumetric flask an amount of powdered tablets equivalent to 0.1 gm. of chloromethapyrilene citrate, fill to the mark with alcohol, and mix thoroughly. Allow the undissolved material to settle, transfer to a second 100 ml. volumetric flask 10 ml. of the clear supernatant liquid, and fill to the mark with alcohol. Mix thoroughly and transfer a 10 ml. portion of this solution to a third volumetric flask and again fill to the mark with alcohol. Determine the absorbancy of the final solution at 2420 Å. The concentration of the final solution in mg./ml. = absorbancy ÷ 41. The amount of chloromethapyrilene citrate present is not less than 95.0 nor more than 105.0% of the labeled amount.

Whittier Laboratories, Chicago.

Tablets Chlorothen Citrate: 25 mg.

Estrone-U.S.P. (See New and Nonofficial Remedies 1952, p. 332).

Carroll Dunham Smith Pharmacal Company, New Brunswick, N. J.

Solution Estrusol in Oil: 1 cc. ampuls and 30 cc. vials. A solution in peanut oil containing 1 mg. of estrone in each cubic centimeter. The 30 cc. vial is preserved with 0.5% chlorobutanol.

Aqueous Suspension Estrusol: 1 cc. ampuls, 5 cc. and 15 cc. vials. A suspension in isotonic saline solution containing 2 mg. of estrone in each cubic centimeter. 5 cc. and 15 cc. vials. A suspension in isotonic saline solution containing 5 mg. of estrone in each cubic centimeter. Preserved with 0.5% chlorobutanol.

Thiamine Hydrochloride-U.S.P. (See New and Nonofficial Remedies 1952, p. 466).

E. R. Squibb & Sons, New York.

Tablets Thiamine Hydrochloride: 3 mg.

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IATROGENIC ADRENAL INSUFFICIENCY

The widespread usefulness of cortisone as a therapeutic agent has resulted in the administration of this hormone to a large number of patients with intact adrenals. Physicians employing cortisone and hydrocortisone (compound F) should be aware of the fact that the continued administration of these agents in doses exceeding 25 mg. per day will in all likelihood induce temporary adrenal atrophy. The larger the dose of cortisone and the longer the period of continued administration the more pronounced will be the degree of adrenal atrophy. It is common practice to use corticotropin to activate the adrenal gland before discontinuing cortisone therapy, although it is recognized that corticotropin improves only the atrophy involving the adrenal cortex and not that of the anterior pituitary.

That symptoms of acute adrenal insufficiency may ensue in certain patients after the discontinuance of cortisone therapy is well established. In the majority of instances, patients recover without undue difficulty. However, were a serious stress such as an operation, acute infection, or traumatic injury to be imposed on a patient during this period of temporary adrenal insufficiency, severe and even fatal consequences might ensue. The recent report of Fraser and associates is a case in point.[1] Physicians not only should bear this possibility in mind and alert patients or their relatives to this danger when cortisone is being withdrawn but should also give serious consideration to the ill effects of imposed stress while the patient is being maintained on long-continued moderate dosage of cortisone or hydrocortisone. Quantitative data indicate that during traumatic injury, operation, or acute infection endogenous adrenal secretion undoubtedly exceeds the equivalent of 50 to 100 mg. of cortisone or hydrocortisone daily; hence, supplementary cortisone or hydrocortisone therapy may be indicated under such circumstances and physicians must be prepared to increase the dose of cortisone above the basal therapeutic level.

Since it has been demonstrated that orally administered cortisone or hydrocortisone is effective almost immediately, supplementary hormone therapy may be given by this route when indicated. Under circumstances in which supplementary oral therapy is not feasible, hydrocortisone or cortisone may be administered intravenously at a rate of 10 to 20 mg. per hour. If care and attention are given to this problem of induced adrenal insufficiency, the untoward effects observed in some patients in the past may be eliminated in the future.

1. Fraser, C. G.; Preuss, F. S., and Bigford, W. D.: Adrenal Atrophy and Irreversible Shock Associated with Cortisone Therapy, J. A. M. A. **149**:1542 (Aug. 23) 1952.

NUMERICAL PREDOMINANCE OF WOMEN OVER MEN IN THE UNITED STATES

For the first time in American history, the 1950 census has shown more women than men in our population, with about 1,430,000 more women than men. Women outnumbered men largely at ages 45 and over, where the sex ratio is 956 men per 1,000 women. This difference increases rapidly with advance in age, and at ages 70 and over it reaches 855 men per 1,000 women. According to present indications, the preponderance of women over men will grow, with an attendant increase in widowhood and dependency.[1]

Various factors contribute to the growing predominance of women over men. Of these, the most important is the higher death rate of males. While the ratio of the two sexes at birth has been stable from year to year, maintaining a level of about 1,055 males per 1,000 females, the ratio of deaths in males to deaths in females nevertheless has been increasing. In 1930 this ratio was 1,210 deaths in males per 1,000 deaths in females, but by 1951 it had risen to 1,333 in males per 1,000 in females. Both sexes have shown a long-term improvement in mortality, with the reduction more rapid among females. Consequently, the gain in population by natural increase (excess of births over deaths) has been greater for females than for males. In the postwar years 1946 through 1951, natural increase added nearly 7 million females to the population of the United States, exceeding the male increment by about 590,000.

This trend, moreover, has been accentuated by the sex pattern of migration into and out of the United States. Although for most of the country's history there has been a marked excess of men over women among immigrants, immigration in each year since 1930 has become predominantly female. During 1932 to 1936, male immigrants were only two-thirds as numerous as female immigrants, while in 1946 there were three females for every male among our immigrants. For the most part, the recent influx of women into the United States reflects the admission of war brides and fiancées of American servicemen.

While fewer men than women have been entering this country each year, more men than women have been leaving our borders. During the early 1930's, male emigrants outnumbered female emigrants by nearly 2 to 1; in no single year was the ratio less than 1½ to 1. For most of the postwar years, however, there has been a relatively small excess of men over women among our emigrants. In the five fiscal years ending June 30, 1950, somewhat more than 13,000 more men than women left the country. During the same period there were 168,500 more women than men among our immigrants. Thus, a net gain of 181,500 women over men has occurred by migration in the five years immediately following World War II.

1. Why Women Outnumber Men, Statist. Bull. Metrop. Life Insur. Co. **33**:1 (Aug.) 1952.

Finally, war deaths have provided an additional factor for widening the margin between our male and female populations. Had it not been for losses sustained in World War II, the present excess of American women over men would be about a third of a million less. The present indications are that this excess will become even larger in the future.

THE BIOSYNTHESIS OF HEMOGLOBIN

The use of isotopes as tracers in studying metabolic processes in the organism has greatly expanded knowledge in this field of science during the past decade. This is particularly true of the problem of the biosynthesis and metabolism of hemoglobin. Studies in which radioactive isotopes of iron were used, either Fe^{55} or Fe^{59}, have demonstrated the remarkable rapidity and completeness of the reutilization of iron from worn-out erythrocytes in the biosynthesis of hemoglobin for new red blood cells.[1] Moreover, again with a radioactive isotope of iron used as a tracer, the locus of the biosynthesis of hemoglobin has been shown to be in the immature erythrocytes of the bone marrow.[2]

Similarly, by the use of isotopes of carbon and nitrogen, a group of investigators at Columbia University [3] has succeeded in demonstrating that the nitrogen of the heme portion of hemoglobin comes from the nitrogen of the amino acid glycine and that the carbon atoms are derived from acetate radicals and glycine. In these investigations, the carbon atoms have been "traced" from glycine and acetates, so that the exact position of the carbon atoms derived from the two precursors in the heme molecule has been determined—one of the outstanding accomplishments in experimental biochemistry of the past decade.

As has been summarized in a recent review [4] globin, the protein portion of the hemoglobin molecule, is synthesized from amino acids derived from dietary protein and from the globin of worn-out erythrocytes. This was first demonstrated in studies on dogs by Whipple and his colleagues [5] and on rats by a group of investigators at Wayne University.[6] Indeed, the latter workers found that a chronic, mild anemia could be produced in rats by the feeding of a diet low in protein. More recently, it was shown in studies [7] in which glycine labelled with radioactive carbon was used, that this substance is used in the biosynthesis of the globin of hemoglobin. Undoubtedly, the same will be found true of other amino acids present in the hemoglobin molecule.

The foregoing studies thus reemphasize the importance of amino acids as well as of iron and simple metabolites such as acetates for the biosynthesis of hemoglobin. The quantitative importance of amino acids in hemoglobin formation is illustrated by the amount of hemoglobin required for daily replacement. It is estimated that 8 gm. of globin is destroyed daily by the average adult.[4] This means, therefore, that approximately 14% of the total dietary protein intake of the average adult is required solely for the resynthesis of new hemoglobin. These data reemphasize the importance of adequate protein, as well as iron, intake for the maintenance of a normal rate of hemoglobin synthesis in man.

DESOXYCORTICOSTERONE ACETATE AND ELECTROLYTE METABOLISM

It is well known that desoxycorticosterone acetate causes a retention of sodium and loss of potassium in both man and experimental animals. But it is not clear whether the potassium deficiency as such can lead to a retention of sodium or whether the sodium retention causes a wasting of potassium. In Addison's disease, in which there is a lack of desoxycorticosterone acetate-like hormone, the serum sodium level falls before an increase in the potassium level occurs.[1]

Recently Fourman and associates [2] studied intensively the changes occurring in the urine and blood electrolytes following administration to a normal subject of desoxycorticosterone acetate. During the test periods, and also during the two control periods, the subject was maintained on a daily intake of 3,000 ml. of water containing 51 mEq. of sodium chloride, 13.4 mEq. of potassium chloride, and 500 gm. of glucose, given in divided doses at two hour intervals around the clock. After the patient was stabilized, urine was collected in two hourly lots for 18 hours, and then in four additional six hourly lots. The effect of the hormone on the electrolyte excretion was determined by comparing the excretion during the identical control period with its paired test period. The latter method was important in making this comparison, since there is a diurnal variation of all substances measured. The excretion of calcium, potassium, sodium, and chloride was lower at night; in contrast, the excretion of ammonium and phosphorus was high at this point. These investigators emphasize the importance of the diurnal variation in electrolytes, particularly when one uses the excretion of one of them as a means of evaluating the results of therapy. During the 42 hours after the administration of the desoxycorticosterone acetate, 48 mEq. of sodium was retained and 14 mEq. of potassium was lost. Calcium and chloride were also retained during this period (45 and 40 mEq. respectively).

There appeared to be no direct cause and effect relationship between the excretion of potassium and the retention of sodium. In fact, sodium retention reached its maximum while potassium excretion was already decreasing, and potassium loss did not follow the variations in sodium retention. Thus, from these studies it appears that desoxycorticosterone acetate has a pronounced effect on sodium metabolism that overshadows and is independent of its action on potassium metabolism.

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2. Walsh, R. J., and others: Iron Metabolism: Heme Synthesis in Vitro by Immature Erythrocytes, Science **110**: 396, 1949.
3. Shemin, D., and Wittenberg, J.: Mechanism of Porphyrin Formation: Rôle of Tricarboxylic Acid Cycle, J. Biol. Chem. **192**: 315, 1951.
4. Drabkin, D. L.: Metabolism of Hemin Chromoproteins, Physiol. Rev. **31**: 345, 1951.
5. Whipple, G. H.: Hemoglobin and Plasma Proteins: Their Production, Utilization, and Interrelation, Am. J. M. Sc. **203**: 477, 1942.
6. Orten, A. U., and Orten, J. M.: Role of Dietary Protein in Hemoglobin Formation, J. Nutrition **26**: 21, 1943.
7. Altman, K. I., and others: Hemoglobin Synthesis from Glycine Labeled with Radioactive Carbon in its *A*-Carbon Atom, J. Biol. Chem. **176**: 319, 1948.

1. Loeb, R. F.: Adrenal Cortex and Electrolyte Behaviour: Harvey Lecture, Bull. New York Acad. Med. **18**: 263 (April) 1942.
2. Fourman, P., and others: Effect of Desoxycorticosterone Acetate on Electrolyte Metabolism in Normal Man, Metabolism **1**: 242 (May) 1952.

ORGANIZATION SECTION

FIFTH ANNUAL MEDICAL PUBLIC RELATIONS CONFERENCE

Hotel Shirley-Savoy, Denver

Monday, December 1, 1952

PROGRAM

REGISTRATION

9:30 A. M., LINCOLN ROOM FOYER

OPENING SESSION

10:00 A. M., LINCOLN ROOM

Chairman: WILLIAM A. LIGGETT, M.D., Denver, President, Colorado State Medical Society

Address of Welcome

GEORGE F. LULL, M.D., Chicago, Secretary and General Manager, American Medical Association

Keynote Address: Medical Public Relations Today

EDWARD J. MCCORMICK, M.D., Toledo, Ohio, President-Elect, American Medical Association

THE INDIVIDUAL DOCTOR IN THE PR PICTURE

10:30 A. M., LINCOLN ROOM

The Before and After of Medical PR (Playlette)

Denver University Players, CAMPTON BELL, Director

Symposium: Public Relations Case Histories

The Discussion of Fees

H. GORDON MACLEAN, M.D., Oakland, Calif., Past President, California Medical Association

Indoctrinating Medical Assistants

OTTO N. GLESNE, M.D., Fort Dodge, Iowa, Chairman, Committee on Public Information and Doctor-Patient Relations, Iowa State Medical Society

Keeping Up-To-Date on Medicine's Activities

W. CLARK BAILEY, M.D., Harlan, Ky., Past President, Kentucky State Medical Association

The Use of Itemized Bills

CHARLES H. RICHARDSON, M.D., Macon, Ga., Past President, Medical Association of Georgia

LUNCHEON

12:15 P. M., EMPIRE ROOM

Toastmaster: DWIGHT H. MURRAY, M.D., Napa, Calif., Chairman, Board of Trustees, American Medical Association

What the People Expect from Their Doctors

ALBERT WILLIAMS SR., Denver,
President, United States National Bank

BUILDING COOPERATIVE PHYSICIAN-HOSPITAL PR PROGRAMS

2:00 P. M., LINCOLN ROOM

Chairman: RAYMOND F. PETERSON, M.D., Butte, Mont., Montana Medical Association

Panel: What constructive public relations activities can be carried on cooperatively by county medical societies and hospitals in their communities?

Moderator: R. A. BENSON, M.D., Bremerton, Wash., Past President, Washington State Medical Association

L. FERNALD FOSTER, M.D., Lansing, Mich., Secretary, Michigan State Medical Society

RICHARD O. CANNON, M.D., Nashville, Tenn., Director, Vanderbilt University Hospital

MRS. ANN FRIEND, Chicago, Public Relations Director, American Hospital Association

DONALD L. MEAMBER, M.D., Yreka, Calif., Siskiyou County Medical Society

BUILDING UNDERSTANDING WITH FUTURE M.Ds

3:30 P. M., LINCOLN ROOM

Panel: What can be done by county medical societies to introduce medical students, interns, and residents to organized medicine . . . and to keep them informed on socioeconomic and public relations activities of interest to the profession?

Moderator: J. LAFE LUDWIG, M.D., Los Angeles, Chairman, Student Relations Committee, Los Angeles County Medical Association

JOHN E. MCDONALD, M.D., Tulsa, Okla., President-Elect, Oklahoma State Medical Association

E. SINKS MCLARTY, M.D., Galveston, Texas, Advisor, Student American Medical Association, University of Texas

LELAND W. HOAR, Salem, Ore., Treasurer, Student American Medical Association

THE YEAR AHEAD

4:30 P. M., LINCOLN ROOM

Presenting the A. M. A.'s 1953 Public Relations Program

LEO E. BROWN, Chicago
Director of Public Relations,
American Medical Association

5:00 P. M., ADJOURNMENT OF CONFERENCE

RECENT A.M.A. PUBLICATIONS

Roster of Executives of State Medical Associations and County Medical Societies and of Editors of County Medical Society Bulletins. Prepared by the Council on Medical Service.

Catalogue of Publications About Your Health, including those of various A.M.A. Councils and Bureaus. Published twice a year.

First Aid Manual. Prepared Jointly by the Council on Industrial Health and the Bureau of Health Education.

New pamphlet on health exhibits available on a loan basis through the Bureau of Exhibits of the A.M.A.

Putting PR to Work—A digest of Proceedings of the First Medical Public Relations Institute. Published by the Public Relations Department.

The AMAzing Story—Designed for the general public, showing how the American Medical Association helps the average American family keep healthy. Published by the Public Relations Department.

Winning Ways with Patients—A public relations handbook for the doctor's secretary showing how to keep the doctor's office running smoothly. Published by the Public Relations Department.

Apparatus Accepted—1952 edition, will be available Dec. 15. This 60-page booklet, published by the Council on Physical Medicine and Rehabilitation, carries a complete listing of diagnostic and therapeutic devices that have been accepted by the Council.

A. M. A. MEMORIAL STONE

Hippocrates will continue without his arms and the Persian King Artaxerxes will have to carry on minus his head. Hippocrates and the Persian king are the central figures in a memorial stone sponsored by the American Medical Association just 100 years ago and placed in the interior wall of the Washington Monument sometime after the Civil War. The physical state of Hippocrates, King Artaxerxes, and his court came to light recently when Dr. Burt L. Davis of Palo Alto, Calif., and his son walked down the steps inside the 550-foot Washington Monument instead of riding on the elevator. At the 240-foot level, they noticed an almost forgotten stone set in the wall. It is one of 188 memorial plaques from states, organizations, and societies paying tribute to Washington.

Carved in bas-relief is a reproduction of the celebrated painting by Girodel Trioson. It shows Hippocrates spurning gifts from Artaxerxes, king of the Persians. The king tried to persuade Hippocrates to practice among the Persians, who were then enemies of the Greeks. At the base of the stone is the Latin inscription *Vincit Amor Patriæ*—Love of country conquers. The heads of three of the figures, including that of the Persian king, had been broken off over the years, and Hippocrates had lost both arms.

On his return home, Dr. Davis wrote the Washington Office of the A. M. A. for further details, and that office then started checking various sources. Files of the National Capital Parks, which has supervision over the Monument, the Armed Forces Medical Library, and the National Archives were combed. The story began unfolding.

At the annual meeting of the A. M. A. in Richmond 100 years ago, a committee was appointed to solicit subscriptions from members for a suitable stone to be placed in the Washington Monument. The committee engaged Lewis Haldy, a marble mason of Lancaster, Pa., and a young sculptor named J. A. Beck to execute the work on a block of Vermont marble. The stone was exhibited at the A. M. A. meeting in 1855 in Philadelphia, and since only half of the fund had been subscribed ($501.30), the Association voted to pay the remainder ($498.70). That same year the stone was delivered to the Washington Monument Society and stored in a "lapidarium" on the Monument grounds. There it remained through the Civil War. Records are a little vague at this point, but, from information at the National Archives, it was deduced that some time between 1885 and 1887 the memorial stone was placed in the Monument.

Next came the question of whether to repair the stone or replace it with a new one. Edward J. Kelly, superintendent of the National Capital Parks, after conferring with other officials, said that since the stone was of such historic value it probably would be best to retain it. A report on the stone subsequently was submitted to the A. M. A. Board of Trustees. They, too, agreed that the stone held too much sentimental and historical significance to be replaced, decapitations and amputations notwithstanding.

COMMISSION ON ACCREDITATION OF HOSPITALS

On Dec. 6, ceremonies marking the joint assumption by the American Medical Association, American College of Physicians, American College of Surgeons, American Hospital Association, and Canadian Medical Association of responsibility for hospital standards will be held in the John B. Murphy Auditorium, 50 E. Erie St., Chicago, at 4 p. m. These organizations form the new Joint Commission on Accreditation of Hospitals, which is located at 600 N. Rush St., Chicago 11. Dr. Edwin L. Crosby, former director of Johns Hopkins Hospital in Baltimore, is executive director of the commission, and Dr. Gunnar Gundersen, La Crosse, Wis., is its first chairman. Principal speaker at the ceremonies will be Sen. Lister Hill of Alabama.

SMALL EXHIBITS FOR LOCAL USE

State and county medical societies may purchase through the A. M. A. Bureau of Exhibits two small suitcase type of exhibits for use in their own communities. One exhibit is devoted to the subject of appendicitis and the other to home accidents. The cost of development, art work, and patterns has been absorbed by the Association. The cost to state and county medical societies represents only the cost of multiple reproduction.

The Association's new exhibit "Health Today" was one of six exhibits awarded a Certificate of Merit at the recent annual meeting of the American Public Health Association in Cleveland.

STATE AMEF CHAIRMEN TO MEET

The official opening meeting for the American Medical Education Foundation's 1953 fund-raising drive will be held Sunday, Jan. 25, at the Sheraton Hotel, Chicago. State chairmen will gather at this second annual meeting to coordinate the medical profession's efforts during the coming year to raise voluntary funds to assist the country's medical schools. (All physicians in the United States will be asked to participate.) The keynote speaker will be L. D. McGuire, M.D., Nebraska drive chairman.

COLLEGE STUDENTS REQUIRED TO READ TODAY'S HEALTH

More than 1,300 freshman physical education students at the University of Illinois at Champaign-Urbana are reading *Today's Health,* published by the A.M.A., as part of their required classroom assignment. As an aid to classroom discussion, a supplementary study sheet called "Classroom Discussion Topics" is being supplied free of charge by the AMA's Bureau of Health Education.

MEDICAL NEWS

ARKANSAS

Cardiac Clinic.—The University of Arkansas School of Medicine in Little Rock has announced a reorganization of the department of cardiology. Under sponsorship of the state department of health and the university medical school, Dr. James E. Doherty, newly appointed director of cardiology and of the heart clinic, and his associates will coordinate all activities. The advisory committee includes Drs. Ralph E. McLochlin, Frederick W. Harris, Oliver C. Melson, Daniel H. Autry, and John N. Compton, all of Little Rock. The clinic accepts only medically indigent patients during the clinic hours each Tuesday and Friday, beginning at 8 a. m.

CALIFORNIA

Survey of Leprosy.—Dr. Jack W. Millar has been loaned by the Navy to the Leonard Wood Memorial Foundation for a year as associate epidemiologist to conduct a survey of leprosy. Dr. Millar previously served as medical director of the leper colony on Tinian Island in the Pacific. His present assignment will take him to Nagashima Island, the Philippines, Siam, India, and Egypt.

Panel Discussion on Hearing Aids.—The ear, nose, and throat section of the San Francisco Medical Society will meet on Nov. 25 at 8:15 p. m. in the society headquarters at 2180 Washington St., for a panel discussion on hearing aids. Dr. Walter P. Work, San Francisco, will speak on "Are Patients Who Need Hearing Aids the Otologists' Problem?" "Modern Concepts of Hearing Aid Selection" and "Hearing Aid Problems in Children" will also be discussed.

Personal.—Dr. Klaus R. Dehlinger, San Francisco, has been appointed associate radiologist at Herrick Memorial Hospital, Berkeley. Dr. Dehlinger was formerly assistant in radiology at the Harvard Medical School, Boston.——Dr. J. Merrill Cruikshank, formerly of Belmont, was recently named Companion of St. Michael and St. George by Queen Elizabeth in formal investiture ceremonies at Buckingham Palace, London. Dr. Cruikshank has been director of medical services in Fiji and inspector-general of the South Pacific Health Service since 1948.

CONNECTICUT

Meeting of Anesthesiologists.—A meeting of the Connecticut State Society of Anesthesiologists will be held in Middletown Nov. 25, when Dr. William S. Derrick, associate in anesthesia, Harvard Medical School, Boston, will discuss "Cortisone, ACTH, and Anesthesia."

GEORGIA

Society News.—At a recent meeting of the Georgia Radiological Society, held in conjunction with the Georgia State Medical Association, the following officers were chosen for the ensuing year: Dr. George M. Hutto, Columbus, president; Dr. Albert A. Rayle Jr., Atlanta, vice-president; and Dr. Robert M. Tankesley, Atlanta, secretary-treasurer.——At its recent annual meeting in Macon, the Georgia Chapter of the American Academy of General Practice presented the following program:

Jason P. Sanders, Shreveport, La., Present Status of the American Academy of General Practice on Good Medical Care.
Paul S. Williamson, Memphis, Future of the General Practitioner.
Andrew S. Tomb, Seminole, Texas, Diagnosis and Treatment of Alcoholism.
Eugene M. Regen, Nashville, Treatment of the Low Back and Sciatic Syndrome.
Major F. Fowler, Atlanta, Diagnosis and Management of Urinary Calculi.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Lecture in Winnetka.—On Dec. 3 Dr. George C. Ham, professor of psychiatry, University of North Carolina School of Medicine, Chapel Hill, will deliver an address on the respiratory system at the North Shore Health Resort, 225 Sheridan Road, Winnetka. This is the third of a series on "Understanding Psychosomatic Disorders."

Swineherd's Disease.—Leptospirosis due to Leptospira pomona, previously reported in cattle and man in Australia and in swine and man in Europe, has been observed among farm animals in several areas of this country, including Illinois. As of Sept. 1, no human cases of leptospiral infection by Lept. pomona had been reported in Illinois. Physicians are urged to be on the alert for the appearance of Lept. pomona infection within the human population. To assist in diagnosis of this disease, procedures are being established in the Division of Laboratories of the Illinois Department of Public Health.

Chicago

Gift for Cardiac Research.—A gift of over $11,000 has been received by the Chicago Medical School from the Meyer Katz Family Foundation for equipping a complete laboratory of cardiac catheterization in the division of cardiovascular research, which is directed by Dr. Aldo A. Luisada. The laboratory will be housed in the Chicago Medical School quarters of the research and professional services building of Mount Sinai Hospital.

Society News.—The Chicago Society of Physical Medicine and Rehabilitation will meet Dec. 3, 8 p. m., at the University of Illinois Medical School (Rm. 106), 1819 W. Polk St., to hear Dr. Frances A. Hellebrandt on "Physiologic Devices for the Facilitation of Work Output in the Rehabilitation of the Disabled." The session will be preceded by dinner at 6 p. m. at Pizzeria Napolitana ($2.75 per plate), 907 Taylor St., and a business meeting.

Sigma Xi Club.—The Sigma Xi club of the Chicago Medical School was installed at Mount Sinai Hospital, Oct. 22. Barry J. Anson, Ph.D., professor of anatomy, Northwestern University Medical School, spoke on "The Story of the Great Plague of London." Officers of the Sigma Xi club of the Chicago Medical School were elected from the faculty as follows: Dr. Piero P. Foa, president; Dr. Israel Davidsohn, vice-president; Leon H. Strong, Ph.D., secretary; and Jay A. Smith, Ph.D., treasurer.

Faculty Appointments.—Recent appointments to the faculty of the Chicago Medical School include Drs. Samuel B. Broder, assistant professor of neurology and psychiatry; Morris A. Kaplan, assistant professor of medicine; Ernest B. Zeisler, associate in medicine; E. Lewin Arendt, instructor in surgery; Meyer J. Barrash, instructor in medicine; Wai-Chi Liu, instructor in surgery; Alex M. Berman, assistant in otolaryngology; Thomas J. Quilty, assistant in otolaryngology; and Antonio N. Silvetti, fellow in surgery. Dr. Aaron Grossman has been advanced to full-time assistant professor of pediatrics.

Honorary Degrees.—In celebration of the 25th anniversary of its medical center (*J. A. M. A.* **150:**40 [Sept. 6] 1952), the University of Chicago bestowed honorary doctor of science degrees on the following persons: Anton J. Carlson, Ph.D., professor emeritus of physiology, University of Chicago, and Dr. Percival Bailey, an alumnus, now professor of neurological surgery at the University of Illinois; Dr. William Bosworth Castle, professor of medicine, and Dr. James L. Gamble, professor emeritus of pediatrics, Harvard Medical School, Boston; Dr. William Smith Tillett, chairman of the department of medicine, New York University College of Medicine; Dr. Allen Oldfather Whipple, Columbia University professor emeritus of surgery; and Dr. George H. Whipple, dean of the University of Rochester (N. Y.) School of Medicine and Dentistry.

KANSAS

University News.—Dr. Mahlon H. Delp has been appointed professor of postgraduate medicine and assistant dean of the University of Kansas School of Medicine, Kansas City. Dr. Delp will continue his duties as professor of medicine. Dr. E. Grey Dimond, associate professor of medicine, has been named chairman of the department of medicine. He will continue with his duties as director of the cardiovascular laboratory.

Appreciation Day.—The community of Scandia recently honored Dr. Charles V. Haggman by presentation of the Dr. Haggman Appreciation Day Program, which included dedication of the library for which Dr. and Mrs. Haggman had given the building and grounds. A basket supper at the school auditorium followed. The evening was devoted to a program in the auditorium, at which Dr. W. Clarke Wescoe, dean of the University of Kansas School of Medicine, Kansas City, delivered an address. A pageant presented by the organizations of Scandia community concluded this celebration at which Dr. Haggman was honored for 50 years of service.

MASSACHUSETTS

Society News.—Dr. Franz J. Ingelfinger, Boston, will present a paper on "Dietary Treatment of Gastroenterological Disorders" before the Norfolk District Medical Society meeting at the Boston Medical Library at 8 p. m., Nov. 25.

Lahey Clinic Lectures.—The following lectures will be held in the Joslin Auditorium, Lahey Clinic, at 7:30 p. m. on the dates given:

Nov. 26, Diseases of the Intestines, Richard B. Cattell and Everett D. Kiefer, Boston.
Dec. 3, Diseases of the Breast, Cornelius E. Sedgwick, Boston. Fluid and Electrolyte Balance, George O. Bell, Boston.
Dec. 10, Hoarseness, Kenneth S. Oliver, Boston. Disease of the Esophagus, Walter B. Hoover, Boston.
Dec. 17, Endoscopy, Kenneth S. Oliver. Vertigo and Deafness, Frank D. Lathrop, Boston.

Lectures in Framingham.—The Middlesex West District Medical Society and the Postgraduate Medical Institute are sponsoring a series of lectures of special interest to general practitioners. The following talks by Framingham physicians, scheduled for December, will be given from 8 to 10 p. m. at the Cushing Veterans Administration Hospital, Framingham. Attendance at the course is open to all physicians.

Dec. 1, Electrolytes and Water Balance, Jack D. Rosenbaum.
Dec. 15, Cortisone and ACTH: Their Application in the Treatment of Disease, Maurice B. Strauss and others.
Dec. 29, Hematuria, William H. Holtham and Herbert S. Talbot.

University News.—Dr. Trygve Gundersen, Boston, formerly chief, division of ophthalmology, Children's Medical Center, has been appointed professor of ophthalmology at Boston University School of Medicine to succeed Dr. Ralph H. Hopkins, whose appointment as professor emeritus follows his retirement. During World War II Dr. Gundersen was chief consultant in ophthalmology to the Surgeon General and the Veterans Administration. He has been assistant clinical professor of ophthalmology at Harvard Medical School and was instructor in ophthalmology and ophthalmic research at the Massachusetts Eye and Ear Infirmary for 15 years.——Boston University School of Medicine announces the retirement of Dr. Louis G. Howard, professor of orthopedic and fracture surgery since 1934, and of Dr. Ralph Harrison Hopkins, professor of ophthalmology since 1944.——Dr. Geoffrey Edsall, professor of microbiology, Boston University School of Medicine, has resigned to become director of the immunology division of the Army Medical Services Graduate School at Walter Reed Army Hospital, Washington, D. C.; and Dr. George L. Maison, head, department of pharmacology at the school of medicine, has resigned to become director of research and development at the Riker Laboratories in Los Angeles. Dr. Earl H. Dearborn, formerly assistant professor of pharmacology at Johns Hopkins University Medical School, Baltimore, has been appointed professor of pharmacology to replace Dr. Maison.——Dr. Maurice B. Strauss, clinical associate in medicine at Harvard Medical School, has been appointed professor of clinical medicine at the Boston University School of Medicine.

MINNESOTA

Course for Gynecologists.—A course in gynecology for specialists will be presented by the University of Minnesota Medical School, Dec. 15-17, on the University Campus, Minneapolis. Subjects to be considered include endometriosis, culdoscopy as a diagnostic tool, and gynecologic malignancy, including the question of carcinoma in situ. Dr. Arthur T. Hertig, professor of pathology, Harvard Medical School, Boston, will participate in the course, which will be presented under the direction of Dr. John L. McKelvey, head of the department of obstetrics and gynecology.

Personal.—Dr. W. Thomas Spain, Minneapolis, has joined the Squibb Institute of Medical Research as director of the Pharmaceutical Research Division.——Dr. Harold S. Diehl, dean of medical sciences and professor of public health in the University of Minnesota Medical School, Minneapolis, and Dr. Albert J. Chesley, secretary and executive officer of the Minnesota State Board of Health since 1921, were recently nominated as honorary members of the Minnesota Public Health Conference for 1952-1953.——Dr. S. Marx White, professor emeritus of medicine, University of Minnesota Medical School, Minneapolis, who last year received the annual distinguished service award of the Community Chest and Council, recently was given the St. Barnabas Bowl, an achievement award in recognition of his medical contribution to the community.——Dr. Wesley W. Spink, professor of medicine, University of Minnesota Medical School, Minneapolis, was called to Spain to advise the government on methods for eradicating brucellosis from livestock. Dr. Spink is director of the Brucellosis Research Center of the World Health Organization.

NEW YORK

Meeting on Neonatal Mortality.—On Nov. 25 Dr. Edith L. Potter, associate professor of pathology in the department of obstetrics and gynecology, University of Chicago, will address the joint meeting of the Medical Society of the County of Erie, the Women Physicians' League of Buffalo, and the Elizabeth Blackwell Society at 9 p. m. at the Hotel Statler, Buffalo. Dr. Potter will discuss neonatal mortality and pathology.

Personal.—Dr. Milton R. Joy of Cazenovia was recently presented with a plaque by the Medical Society of the County of Madison, of which he has been a member for 66 years.——Dr. Nathan Beckenstein, director of Syracuse Psychopathic Hospital, was recently transferred to Brooklyn State Hospital as director, succeeding the late Dr. Clarence H. Bellinger. Dr. Richard F. Binzley, associate director of Pilgrim State Hospital, West Brentwood, has been appointed to replace Dr. Beckenstein at Syracuse.

Lectures on Rheumatic Fever.—At the meeting of the Masonic Research Foundation on Rheumatic Fever at Syracuse Academy of Medicine, Nov. 24 at 8:30 p. m., the following program will be presented:

Homer F. Swift, New York, Major Problems in Rheumatic Fever.
Ralph H. Boots, New York, Juvenile Rheumatoid Arthritis.
Charles A. Ragan, New York, Current Status of Treatment of Rheumatoid Arthritis.
Currier McEwen, New York, Current Status of Treatment of Rheumatic Fever.
John H. Talbott, Buffalo, Newer Therapeutic Agents in Treatment of Gout.

Course in Ophthalmology.—The department of ophthalmology of the State University of New York Medical Center at Syracuse will present its third annual postgraduate course in ophthalmology at the Hotel Syracuse, Dec. 5-6. The following lecturers will participate: Dr. Albert D. Ruedemann, Detroit, Dr. F. Bruce Fralick, Ann Arbor, Mich., Dr. Harold G. Scheie, Philadelphia, and Dr. Raynold N. Berke, Hackensack, N. J. The tuition fee ($25 payable to the State University of New York Medical Center at Syracuse, Irving Ave., Syracuse) covers tuition, daily luncheons, and dinner Friday night. The course will be limited to 60 members. Inquiries may be addressed to Dr. Harold H. Joy, 504 State Tower Bldg., Syracuse.

New York City

Macy Foundation Moves.—The Josiah Macy Jr., Foundation has moved to 16 W. 46th St., Botany Building, New York 36. The phone number is PLaza 7-7705.

Schoenberg Lecture.—Dr. Charles L. Schepens of Boston will deliver the annual Mark J. Schoenberg lecture at the New York Academy of Medicine, Dec. 1, on "The Prognosis and Treatment of Retinal Detachment." This lectureship, established as a memorial to the late Dr. Schoenberg's interest in the prevention of blindness, is sponsored by the National Society for the Prevention of Blindness and the New York Society for Clinical Ophthalmology.

Monthly Meetings on Therapeutics.—The New York Academy of Medicine is presenting monthly panel discussions on therapeutics. The subjects, which deal with practical and specific problems confronting the practicing physician, will be presented on Fridays at 4:30 p. m. as follows:

Dec. 5, Hepatitis and Cirrhosis of the Liver, Moderator, Franklin M. Hanger.
Jan. 9, 1953, Hypertensive Vascular Diseases, Moderator, William Goldring.
Feb. 6, Disorders of the Blood, Moderator, Claude E. Forkner.
March 6, The Failing Heart, Moderator, Charles E. Kossmann.
April 3, Rheumatic Fever and Rheumatoid Arthritis, Moderator, Charles A. Ragan.

Dr. Allen Whipple Honored.—About 300 persons recently attended a dinner at the Hotel Plaza, given by former members of the surgical house staff of the Presbyterian Hospital to honor Dr. Allen O. Whipple, who for 25 years (1921-1946) served as Valentine Mott professor of surgery at the Columbia University College of Physicians and Surgeons and as director of the surgical service of the Presbyterian Hospital. A portrait of Dr. Whipple was presented to the hospital. Dr. George H. Humphreys II, who succeeded Dr. Whipple as director of surgical service at the Columbia-Presbyterian Medical Center, announced the organization, by alumni, of the Allen O. Whipple Society to honor distinguished contributors to the science of surgery. Speaker of the evening was Dr. Wilder G. Penfield, professor of neurology and neurosurgery at McGill University, Montreal, Canada. Dr. Whipple was president of the New York Surgical Society, the Society for Clinical Surgery, and the American Surgical Association, and chairman of the American Board of Surgery. He has been editor-in-chief of "Nelson's Loose-Leaf Surgery" and a member of the editorial board of *Annals of Surgery*. During World War II he served as chairman of the subcommittee on infected wounds and burns, National Research Council, and as a consultant in England and North Africa.

OHIO

Heart Association Opens Office.—The Ohio Heart Association has opened a full-time office in Columbus at 55 E. State St., Rm. 601. Current officers of the association are: Dr. Bernard A. Schwartz, Cincinnati, president; Dr. Maurice A. Schnitker, Toledo, vice-president; Mr. L. A. Seikel, Akron, secretary; and Mr. Charles W. McCoy, Columbus, treasurer. Mr. Walter S. Page Jr. is executive secretary.

Dr. Meiling Honored.—Dr. Richard L. Meiling, associate dean, Ohio State University College of Medicine, Columbus, recently received the Academic Robes of the Faculty of Medicine of the University of Munich, this being the first time in many years that the faculty has voted to award these robes to a nonfaculty member. Dr. Meiling presented a paper discussing "The Use of Radioactive Substances in Treating Cancer of the Cervix at Ohio State University Hospital" before the European Assembly of the 29th Congress of the German Gynecological Society in Munich.

Personal.—Dr. Benjamin S. Kline, originator of the Kline test for the detection of syphilis, has announced his resignation as chief of Mount Sinai Hospital's department of laboratories, Cleveland, a position he has held since 1923.——Dr. Robert W. Heinle, associate professor of medicine, Western Reserve University School of Medicine, Cleveland, has joined the medical division of the Upjohn Company, Kalamazoo, Mich. He was formerly affiliated with the University Hospitals of Cleveland, Boston City Hospital, and Harvard Medical School, Boston.——Dr. Gordon B. Munson, Dayton, was recently awarded lifetime membership in the Ohio Congress of Parents and Teachers for his work in school health.——Dr. John D. Porterfield, Columbus, was recently appointed by Gov. Lausche to a second five year term as director of health for Ohio. Dr. Porterfield was associated with the U. S. Public Health Service from 1939 to 1947.

OKLAHOMA

Address on Chronic Urinary Tract Infections.—Dr. Vincent D. Vermooten, associate professor of urology at Southwestern Medical School of the University of Texas, Dallas, Texas, will address the Tulsa Academy of General Practice, Nov. 24 at 8 p. m., at the Hotel Tulsa on "Management of Chronic Urinary Tract Infections."

OREGON

State Medical Election.—At its annual session in Portland the Oregon State Medical Society installed Dr. John D. Rankin of Coquille as president and chose Dr. J. Milton Murphy, Portland, as president-elect. Dr. Charles E. Littlehales, Portland, was named secretary, and Dr. Robert W. Kullberg, Portland, was reelected treasurer.

Honor Oregon's Oldest Physicians.—At its annual banquet the Oregon State Medical Society presented scrolls to its two oldest active members, Dr. George Elva Houck, Roseburg, aged 86, and Dr. William Horsfall, Coos Bay, aged 85, each of whom has been in continuous practice for more than 60 years. Dr. Houck, who in 1934 was elected to honorary membership in the Oregon State Medical Society, has served as president of the Southern Oregon Medical Society and as councilor of the state society. He has been president of the state board of health and a member of Roseburg's City Council and later its mayor. Dr. Horsfall has twice served as president of the Coos-Curry County Medical Society, was once county coroner, and in 1939 was elected as First Citizen of Coos Bay.

TENNESSEE

Physicians to Select Postgraduate Courses.—Midsouth physicians are being given an opportunity to select the postgraduate courses to be offered by the University of Tennessee Medical Units. Inquiries have been sent to all Tennessee physicians and others within a 150 mile radius of Memphis in Arkansas, Alabama, Missouri, Kentucky, and Mississippi by a committee consisting of Drs. William T. Satterfield, Memphis, representing the Tennessee Academy of General Practice and the local chapter, Nicholas Gotten, member of the Memphis and Shelby County Medical Society, and J. Paul Baird, Dyersburg, representing the Tennessee State Medical Association.

TEXAS

New Outlying Divisions of Graduate School.—Divisions of the University of Texas Postgraduate School of Medicine have been formally established in Tyler and Corpus Christi by the board of regents. Dr. J. Weldon Birdwell was appointed director of the Tyler division, and the Mother Frances Hospital in Tyler was approved as an affiliate hospital of the postgraduate school. Dr. Kleberg Eckhardt has been named director of the Corpus Christi division, and the affiliate hospitals in that city are the Spohn Hospital, the Memorial Hospital, and the Driscoll Foundation Children's Hospital. In Houston the postgraduate school of medicine recently completed an affiliation agreement with Memorial Hospital.

WASHINGTON

Multiple Sclerosis Clinic.—The new $250,000 multiple sclerosis clinic building at St. Joseph's Hospital in Tacoma was recently dedicated. All facilities and equipment have been planned for the convenience of multiple sclerosis patients. Dr. Hinton D. Jonez is the founder of the clinic, and, in appreciation of his work, the Sisters of St. Francis underwrote the cost of construction of the clinic.

GENERAL

Award for African Sleeping Sickness Cure.—The government of Belgium has revived a 46 year old royal decree offering an award of $20,000 to the discoverer of a cure for African sleeping sickness. According to Maurice Iweins d'Eeckhoutte, Belgian consul general in Chicago, no machinery was set up to select a winner when the original decree was issued in 1906. A four man committee of judges has been appointed.

New Geriatrics Publication.—The American Geriatrics Society announces the forthcoming publication of their official periodical, *Journal of the American Geriatrics Society*. The new journal will be edited by Dr. Willard O. Thompson of Chicago, president of the society. Membership in the society is open to physicians interested in diseases of the aging. Information may be obtained from the permanent secretary, Dr. Malford W. Thewlis, Wakefield, R. I.

Clinic Administrators to Meet in St. Louis.—The second annual meeting of the American College of Clinic Administrators will be held at the Chase Hotel, St. Louis, Dec. 6-7. During the Saturday morning session Dr. Cecil A. Z. Sharp, area medical director, United Mine Workers of America, St. Louis, will speak on "Health Services Provided Beneficiaries of the U. M. W. A. Welfare and Retirement Fund." The annual banquet, which will be held at 7 p. m., will be addressed by Dr. Homer D. Junkin, Paris, Ill.

Mental Health Clinics for Children.—The National Institute of Mental Health reports that 1,228 mental health clinics are now operating in the United States and that almost 75% of them are partly or entirely devoted to serving children. Almost half of all clinics are located in cities having 100,000 or more inhabitants. About two-thirds of the clinics are operated primarily outside of hospital settings; less than one-fourth are located in general hospitals; and 14% are in mental hospitals. About 11% of the clinics provide diagnostic service only.

Medical Women to Meet at the Broadmoor.—The American Medical Women's Association will hold its midyear meeting at the Broadmoor Hotel, Colorado Springs, Colo., Nov. 29 to Dec. 1 under the presidency of Dr. Evangeline E. Stenhouse, Chicago. Dr. Carroll C. LaFleur Birch, Chicago, who was the acting head of Lady Hardinge Medical School, New Delhi, India, during the past year, will address the Sunday evening banquet on "A Year in India." An award of merit will be given to the graduating medical woman who had the highest scholastic average during her four years of medicine.

Antituberculosis Vaccination.—According to the UN Department of Public Information, 7,255,122 children and young adults in 15 countries and territories of Latin America, the Eastern Mediterranean, Southeast Asia, and the Western Pacific have been tested for tuberculosis and 3,512,761 of them have been vaccinated, with the aid of WHO and UNICEF in new projects launched since the end of the International Tuberculosis Campaign in June, 1951. Some 29 million children and young adults were tested in 22 countries and 14 million of them vaccinated during the international campaign.

Contributions for Anesthesia Library.—Members of the department of anesthesiology, University of Iowa Hospitals, Iowa City, have established a memorial library in honor of Dr. Donald S. Wilkins, who died from poliomyelitis while he was serving in Korea. The trustees of the Wilkins Memorial Library of Anesthesia are interested in the acquisition of worthwhile books or reprints and of anesthetic apparatus of historic value. Persons knowing of the availability of such items or of collections that are for sale are asked to communicate with Dr. Lucien E. Morris, Division of Anesthesiology, University Hospitals, Iowa City.

Mobile Physiotherapy Units.—Four chapters of the National Arthritis and Rheumatism Foundation (in Arizona, Northern California, Michigan, and the District of Columbia) have set up mobile units that enable physiotherapists to take portable equipment to the homes of rheumatic disease patients. A similar project is in operation in Canada, where the Canadian Arthritis and Rheumatism Society has 30 mobile units servicing more than 24 scattered cities in 7 provinces. Programs both in the United States and Canada provide for adjustment of the cost according to the patient's ability to pay, with the society or foundation making up the deficit.

Rotary International District Governors.—Four physicians have been named district governors of Rotary International for 1952-1953. They are Drs. William O. Callaway, Burlingame, Calif.; Benjamin N. Saltzman, Mountain Home, Ark.; Howard O. Smith, Marlin, Texas; and John C. Wiedenmann, Englewood, Colo. As district governors they coordinate activities of all Rotary clubs in their districts. During the year, they will visit each club to offer advice in club administration and service work, which includes community betterment, promotion of high standards in business and professions, and the advancement of international understanding, good will, and peace.

Proctology Award Contest.—The International Academy of Proctology has announced its annual cash prize and certificate of merit award contest for 1952-1953. The best unpublished contribution on proctology or allied subjects will be awarded $100 and a certificate of merit. This competition is open to all physicians in all countries. Awards will be made at the annual convention dinner dance of the International Academy of Proctology in May, 1953. The academy reserves the exclusive right to publish all contributions in the *American Journal of Proctology and Gastroenterology*. All entries are limited to 5,000 words, must be typewritten in English, submitted in five copies, and received no later than April 1, 1953. Entries should be addressed to the International Academy of Proctology, 43-55 Kissena Blvd., Flushing 55, N. Y.

Fellowships in Public Health and Preventive Medicine. — The National Foundation for Infantile Paralysis announces the availability of a limited number of postdoctoral fellowships in the field of public health and preventive medicine. The fellowships are for one or more years at an approved school of public health, with a period of field experience when arranged by the school. Fellowships may cover tuition, maintenance, and an allowance for books, if required. An appropriation of $330,600 in March of Dimes funds has been made for this program. Eligibility requirements include United States citizenship, sound health, graduation from an approved medical school, and completion of at least a one year internship in an approved hospital. Information may be obtained from the Division of Professional Education, National Foundation for Infantile Paralysis, 120 Broadway, New York 5.

Pathologists Meeting in Chicago.—The North Central Region College of American Pathologists, the Illinois Society of Pathologists, and the American Academy of Forensic Sciences will meet at the Drake Hotel, Chicago, Dec. 6. The following papers will be presented:

Walter J. R. Camp, Chicago, Toxicology of Barbiturates.
Jerry J. Kearns, Chicago, What the Pathologist Should Know in Performing a Medical Legal Necropsy.
Ralph F. Turner, B.S., East Lansing, Mich., Role of the Police Scientist in a Medical Legal Investigation.

In the afternoon a tissue seminar will be held from 1:30 to 4 p. m. under the sponsorship of the Illinois Society of Pathologists. Those who wish to receive slides and abstracts of case histories are requested to communicate with Dr. Franklin J. Moore, Secretary, Illinois Society of Pathologists, 55 E. Washington St., Chicago. There will be an attendance fee of $1 except for residents and those still in training.

Annual Blakeslee Award Contest.—The American Heart Association has announced the rules for the first annual Howard W. Blakeslee award (*J. A. M. A.* **149**:879 [June 28] 1952). A prize of $1,000 will be given to the person whose creative efforts in scientific reporting have contributed most toward public understanding of cardiovascular disease in any medium of communication. Material published or produced during the 1952 calendar year is eligible for consideration. Entries must be postmarked not later than Jan. 15, 1953. The winner will be announced at the annual meeting of the American Heart Association, in April, 1953, in Atlantic City. Information may be obtained from the Managing Committee, Howard W. Blakeslee Award, American

Heart Association, 44 E. 23rd St., New York 10. The award was made possible through funds contributed by the Industrial Publishing Company of Cleveland and the Robert Z. Greene Foundation of New York City.

Chest Physicians Offer Award.—The board of regents of the American College of Chest Physicians offers a cash prize of $250 to be given annually for the best original contribution, preferably by a young investigator, on any phase relating to chest disease. The prize is open to contestants of all countries. Manuscripts submitted become the property of the American College of Chest Physicians and will be referred to the editorial board of its journal, *Diseases of the Chest*, for consideration. The college reserves the right to invite the winner to present his contribution at the annual meeting. The following conditions must be observed: 1. Five copies of the manuscript, typewritten in English, should be submitted to the executive office, American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, not later than March 15, 1953. 2. The only means of identification of the author or authors shall be a motto or other device on the title page and a sealed envelope bearing the same motto on the outside, enclosing the name of the author or authors.

Conference on Nucleonics in Medicine. — At the fifth annual Conference on Electronic Instrumentation and Nucleonics in Medicine at the New Yorker Hotel, New York, Nov. 24-25, 18 technical papers will be presented. The conference will consider the development, design, and application of instruments intended to facilitate medical research and everyday use by physicians or medical technicians. On Monday electronic instrumentation in medicine, including methods of measurement, analysis of data, and a number of electronic instruments and accessories important in the medical field, will be discussed. Nucleonics in medicine, presented Tuesday, will include papers on isotope measuring techniques, the use of nuclear instruments, and effects of radiation. Dr. Eugene L. Saenger and Dr. Ji-Toong Ling, University of Cincinnati College of Medicine, will discuss "Medical Applications of Ohmart Cells" on Tuesday morning, and Tuesday afternoon Drs. Roger A. Harvey and Lewis L. Haas of the University of Illinois, Chicago, will present a paper on "Technical Aspects of the High-Energy Electron Beam Used in Therapy."

Academy of Dermatology and Syphilology. — The American Academy of Dermatology and Syphilology will hold its annual meeting Dec. 6-11 at the Palmer House, Chicago, under the presidency of Dr. C. Guy Lane, Boston. Special courses in histopathology, mycology, x-ray and radium therapy, bacteriology of the skin, anatomy and embryology, special problems in dermatohistopathology, and research methods in dermatology will be held Saturday and Sunday. Thirty-six informal discussion groups are scheduled for noon and afternoon meetings and on Wednesday there will be seven informal panel discussions on special dermatological subjects. The following special lectures will be given:

Erythema Multiforme Group of Bullous Disorders, Clinton W. Lane, St. Louis.
Etiology and Treatment of the Toxic Bullous Dermatoses, Frank C. Combes, New York.
Urticaria—Due to Food or Nerves? Walter C. Alvarez, Chicago.
Treatment of Malignancy of the Face, Mouth, and Neck by the Radiologist, Charles L. Martin, Dallas.
Sunlight and Cancer of the Skin, Harold F. Blum, Ph.D., Princeton, N. J.

On Tuesday from 2 to 4 p. m. there will be a panel discussion on "Diagnosis and Treatment of Cutaneous Malignancy." Symposiums are scheduled on the following subjects: internal medical aspects of cutaneous disease, mucous membrane lesions, physical and radiation therapy, physiology and chemistry of the skin, cutaneous granulomas, industrial dermatoses, cutaneous malignancy, syphilis, history of dermatology, miscellaneous dermatoses, pharmaceutical therapeutics, and surgical management of dermatological lesions. The annual banquet will be held at 7:30 p. m. Wednesday.

Award to Dr. Maxcy.—At its annual meeting in Cleveland the American Public Health Association bestowed on Dr. Kenneth Fuller Maxcy, professor of epidemiology, Johns Hopkins University School of Medicine, Baltimore, the Sedgwick Memorial Medal for his achievements in research and teaching and his contributions to the understanding of typhus. The citation reads in part as follows: "Dr. Maxcy's career in the United States Public Health Service extended over eight years, ending in 1929, during which he attained the rank of surgeon. He conducted epidemiological studies on malaria in the Southern United States, representing his country in conferences in Geneva. During this period he also began his epidemiological and laboratory studies of endemic typhus in the United States establishing for the first time the life cycle of this organism in its relationships to the rat and flea. This was the beginning of a life-long interest in the rickettsial diseases." Dr. Maxcy has served the Rockefeller Foundation for many years as consultant and, since 1941, has been consultant to the Army Epidemiological Board and to the Research and Development Board of the military establishment.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories, and possessions in the weeks ended as indicated:

Area	Nov. 1, 1952	Oct. 25, 1952	Nov. 3, 1951
New England States			
Maine	8	5	..
New Hampshire	2	4	..
Vermont	3	1	..
Massachusetts	18	26	2
Rhode Island	2	9	1
Connecticut	6	13	4
Middle Atlantic States			
New York	84	120	53
New Jersey	30	29	13
Pennsylvania	56	68	13
East North Central States			
Ohio	122	140	38
Indiana	31	55	4
Illinois	126	161	32
Michigan	121	162	49
Wisconsin	79	84	45
West North Central States			
Minnesota	146	156	23
Iowa	143	138	8
Missouri	33	39	47
North Dakota	10	17	6
South Dakota	49	49	1
Nebraska	37	98	9
Kansas	65	67	28
South Atlantic States			
Delaware	2	3	1
Maryland	20	9	1
District of Columbia	..	2	1
Virginia	13	17	4
West Virginia	21	17	14
North Carolina	22	24	4
South Carolina	7	21	1
Georgia	11	6	17
Florida	18	34	1
East South Central States			
Kentucky	33	48	..
Tennessee	10	25	22
Alabama	5	5	16
Mississippi	12	7	23
West South Central States			
Arkansas	7	14	8
Louisiana	17	31	8
Oklahoma	15	30	9
Texas	26	32	46
Mountain States			
Montana	12	6	5
Idaho	13	18	14
Wyoming	7	2	12
Colorado	14	18	19
New Mexico	13	9	13
Arizona	19	15	7
Utah	56	20	13
Nevada	6	2	1
Pacific States			
Washington	47	46	18
Oregon	26	22	26
California	197	191	125
Territories and Possessions			
Alaska	3	10	..
Hawaii	2	1	..
Puerto Rico	6	..	2
Total	1,820	2,126	806

Society News. — Officers of the American Medical Women's Association for 1952-1953 are Dr. Evangeline E. Stenhouse, Chicago, president; Dr. Judith E. Ahlem, Livermore, Calif., president-elect; Dr. Leslie S. Kent, Eugene, Ore., first vice-president; Dr. Katharine W. Wright, Evanston, Ill., recording secretary; and Dr. Elizabeth H. R. Fischer, Chicago, corresponding secretary.——At the annual meeting of the College of American Pathologists in Chicago, Dr. William A. D. Anderson of Milwaukee was elected vice-president, to assume office on Jan. 1, 1953, at which time Dr. David A. Wood of San Francisco, currently vice-president and president-elect, will begin his three year term as president.——At the annual meeting of the American Society of Maxillofacial Surgeons in San Diego, Calif., Dr. John W. Gerrie, Montreal, Canada, was elected president; Dr. William F. Harrigan, New York, vice-president; Dr. Casper M. Epsteen, Chicago, secretary-treasurer; and Dr. James O. Beavis, Dayton Ohio, member of the Board of Trustees. —— The following officers were elected by the Association of American Physicians: Dr. William S. McCann, Rochester, N. Y., president; Dr. Joseph T. Wearn, Cleveland, vice-president; Dr. W. Barry Wood Jr., St. Louis, secretary; Dr. Francis C. Wood, Philadelphia, treasurer; and Dr. Cecil J. Watson, Minneapolis, recorder.——At the annual meeting of the American Electroencephalographic Society Dr. Robert B. Aird, San Francisco, was elected president; Mary A. B. Brazier, Ph.D., Boston, president-elect; Dr. John A. Abbott, Boston, secretary; and Charles E. Henry, Ph.D., Hartford, Conn., treasurer.——At its annual meeting in New York, the American Congress of Physical Medicine elected Dr. Walter M. Solomon, Cleveland, president; Dr. William B. Snow, New York, president-elect; Dr. Frances Baker, San Mateo, Calif., secretary; Dr. Frank H. Krusen, Rochester, Minn., treasurer; Dr. Walter J. Zeiter, Cleveland, executive director; and Mrs. Dorothea C. Augustin, executive secretary.

LATIN AMERICA

Insect Control Programs.—According to a World Health Organization report, between July, 1950, and June, 1952, insect control programs were undertaken in British Honduras, Costa Rico, El Salvador, Guatemala, Honduras, and Nicaragua by the governments with technical advice from WHO and with supplies provided by the United Nations International Children's Emergency Fund. The projects were directed against such insect-borne diseases as malaria, yellow fever, and typhus. The protection afforded was given at a cost of 26 cents per person.

FOREIGN

Conference on Child Welfare. — An International Study Conference on Child Welfare will be held in Bombay, India, Dec. 5-12. The general theme will be "Child Welfare in Relation to Social Services and the Raising of Standards of Living." Dr. Henry H. Kessler, Newark, N. J., member of the council of the International Society for the Welfare of Cripples, will be chairman of a special session to consider "Care and Education of the Physically Handicapped Child."

Antimalaria Campaigns.—At a cost of slightly more than 10 cents per person, 1,117,236 men, women, and children were protected against malaria in five experimental areas of Thailand and India in demonstrations conducted by the World Health Organization and the United Nations International Children's Emergency Fund, 1949-1951. In the Terai, malaria transmission is reported to have been definitely stopped. Following malaria control measures, the area under cultivation was increased and, according to local residents, land values have almost doubled.

CORRECTION

Treatment of Bronchial Asthma.—In the paper by this title in THE JOURNAL, Oct. 11, 1952, in the third line of the last paragraph on page 565, the word "or" should be inserted after the word intravenously.

Inguinal Hernia in Infants and Children.—Under this title in the Brazil foreign letter, in THE JOURNAL, Nov. 1, 1952, page 949, the word "men" should have been "males" and the word "women" should have been "females."

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 23-25. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery.

ALASKA:* *Examination.* Juneau, March 3. On application in other towns where there are board members. *Reciprocity.* On application. Sec., Dr. W. M. Whitehead, Box 140, Juneau.

COLORADO:* *Examination.* Denver, Jan. 13-16. Exec. Sec., Mrs. B. H. Hudgens, 831 Republic Bldg., Denver.

CONNECTICUT:* *Regular. Examination.* Hartford, Nov. 12-13. Sec. to the Board, Dr. Creighton Barker, 160 St. Ronan St., New Haven. *Homeopathic.* Derby, Nov. 11-12. Sec., Dr. Donald A. Davis, 38 Elizabeth St., Derby.

DELAWARE: *Examination.* Dover, Jan. 13-15. *Reciprocity.* Dover, Jan. 22. Sec., Dr. J. S. McDaniel, 229 South State St., Dover.

DISTRICT OF COLUMBIA:* *Examination.* Washington, Nov. 10-12. Sec., Dr. Daniel L. Seckinger, 4130 E. Municipal Bldg., Washington.

FLORIDA:* *Examination.* Jacksonville, Nov. 23-25. Sec., Dr. Homer L. Pearson, 701 Dupont Bldg., Miami 32.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agana.

HAWAII: Honolulu, Jan. 12-14. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: Boise, Dec. 12-14. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

INDIANA: *Examination.* Indianapolis, June 23-25. Ex. Sec., Miss Ruth V. Kirk, 538 K of P Bldg., Indianapolis.

IOWA:* *Examination.* Des Moines, Dec. 8-10. Acting Director, Dr. Walter L. Bierring, State Office Bldg., Des Moines.

KANSAS: Topeka, Dec. 10-11. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, Dec. 8-10. Sec., Dr. Bruce Underwood, 620 S. 3rd St., Louisville.

MAINE: Portland, Nov. 12-13. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, Dec. 9-12. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1.

MASSACHUSETTS: *Examination.* Boston, Jan. 13-16. Sec., Dr. Robert C. Cochrane, Room 37, State House, Boston.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., Dr. R. N. Whitfield, State Board of Health, Jackson 113.

NEBRASKA:* *Examination.* Omaha, June 1953. Director, Mr. Husted K. Watson, Room 1009 State Capitol Bldg., Lincoln 9.

NORTH CAROLINA. *Reciprocity.* Winston Salem, Jan. 19. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, Jan. 7-9. *Reciprocity.* Grand Forks, Jan. 10. Sec., Dr. C. J. Glaspel, Grafton,

PENNSYLVANIA: *Examination.* Philadelphia, January. Acting Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

SOUTH CAROLINA: *Examination.* Columbia, Nov. 10-11. Sec., Mr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* Sioux Falls, Jan. 20-21. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

TEXAS:* *Examination.* San Antonio, Nov. 13-15. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Ft. Worth.

UTAH: *Examination.* Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City.

VIRGINIA: *Examination.* Richmond, Dec. 11-13. *Reciprocity.* Richmond, Dec. 10. Sec., Dr. K. D. Graves, 631 First St., S.W., Roanoke, Va.

WISCONSIN: *Examination.* Madison, January 13-15. Sec., Dr. A. G. Koehler, 46 Washington Blvd., Oshkosh.

VIRGIN ISLANDS: *Examination.* St. Thomas, Nov. 12-13. Sec., Dr. Earle M. Rice, St. Thomas.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: *Examination.* On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

OKLAHOMA: Oklahoma City, April 3. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, Dec. 6. Sec., Dr. Charles D. Byrne, State Board of Higher Education, University of Oregon, Eugene.

RHODE ISLAND: Providence, Nov. 12. Admin. of Professional Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: *Examination.* Vermillion, Dec. 5-6. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

WISCONSIN: *Examination.* Milwaukee, Dec. 6. Madison, April 11. Sec., Mr. W. H. Barber, 621 Ransom St., Ripon.

* Basic Science Certificate required.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1952 Clinical Session, Denver, Dec. 2-5.

1953 Annual Session, New York, June 1-5.

1953 Clinical Session, St. Louis, Dec. 1-4.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY, Palmer House, Chicago, Dec. 6-11. Dr. John E. Rauschkolb, P.O. Box 6565, Cleveland 1, Secretary.

AMERICAN ACADEMY OF OBSTETRICS AND GYNECOLOGY, Palmer House, Chicago, Dec. 15-17. Dr. Ralph A. Reis, 116 S. Michigan Blvd., Chicago 3, Secretary.

AMERICAN ASSOCIATION OF MEDICAL CLINICS, Cosmopolitan Hotel, Denver, Nov. 30-Dec. 1. Dr. Edwin P. Jordan, Box 114, Charlottesville, Va., Executive Director.

AMERICAN COLLEGE OF CLINIC ADMINISTRATORS, Chase Hotel, St. Louis, Dec. 6-7. Dr. Eva M. Rule, 106 North Silver Street, Olney, Ill., Secretary.

AMERICAN PSYCHOANALYTIC ASSOCIATION, New Yorker Hotel, New York, Dec. 4-7. Dr. LeRoy M. A. Maeder, 1910 Rittenhouse Square, Philadelphia 3, Secretary.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASES, Hotel Roosevelt, New York, Dec. 12-13. Dr. Clarence C. Hare, 700 West 168th St., New York 32, Secretary.

ASSOCIATION OF STATE AND TERRITORIAL HEALTH OFFICERS, Washington, D. C., Dec. 8-11. Dr. John D. Porterfield, 306 Ohio Depts. Bldg., Columbus 15, Ohio, Secretary.

EASTERN SECTION, American Laryngological, Rhinological and Otological Society, Hotel Syracuse, Syracuse, N. Y., Jan. 7. Dr. Francis W. Davison, Danville, Pa., Chairman.

NORTHWEST SOCIETY FOR CLINICAL RESEARCH, Seattle, Jan. 16-17. Dr. Arthur L. Rogers, 1216 S.W. Yamhill St., Portland 5, Ore., Secretary.

PUERTO RICO MEDICAL ASSOCIATION, Santurce, Dec. 10-14. Dr. Luis R. Guzman-Lopez, Box 9111, Santurce, Secretary.

RADIOLOGICAL SOCIETY OF NORTH AMERICA, Netherland Plaza and Sheraton-Gibson Hotels, Cincinnati, Dec. 7-12. Dr. Donald S. Childs, 713 East Genesee St., Syracuse 2, N. Y., Secretary.

SOUTHERN SECTION, AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, Andrew Jackson Hotel, Nashville, Tenn., Jan. 12. Dr. Lester A. Brown, 490 Peachtree St., N.E., Atlanta 3, Ga., Chairman.

SOUTHERN SURGICAL ASSOCIATION, Hollywood, Fla., Dec. 9-11. Dr. John C. Burch, 2112 West End Ave., Nashville 5, Tenn., Secretary.

WESTERN SURGICAL ASSOCIATION, The Shamrock, Houston, Texas, Dec. 4-6. Dr. Michael L. Mason, 154 East Erie St., Chicago 11, Secretary.

INTERNATIONAL

CONGRESS OF INTERNATIONAL LEAGUE AGAINST RHEUMATISM, Geneva and Zurich, Switzerland, Aug. 24-29, 1953. For information write: Dr. W. Tegner, The London Hospital, London E.1, England.

CONGRESS OF THE INTERNATIONAL SOCIETY OF SURGERY, Lisbon, Portugal, Sept. 15-20, 1953. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

INTER-AMERICAN SESSION, American College of Surgeons, Paulista Medical Association Bldg., Sao Paulo, Brazil, Feb. 9-12, 1953. Dr. Moacyr Eyck Alvaro, 1151 Conselacao, Sao Paulo, Brazil, Chairman.

INTERNATIONAL CONGRESS OF AUDIOLOGY, Groningen, Netherlands, June 5-6, 1953. Dr. Gunnar Holmgren, Strandvagen 5A, Stockholm, Sweden, President.

INTERNATIONAL CONGRESS OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY, Boston, Mass., U. S. A., Aug. 18-21, 1953. Dr. Robert S. Schwab, Massachusetts General Hospital, Boston 14, Mass., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS FOR HISTORY OF SCIENCE, Jerusalem, Israel, August 3-7, 1953. Prof. F. S. Bodenheimer, Hebrew University, Jerusalem, Israel, President.

INTERNATIONAL CONGRESS ON MEDICAL LIBRARIANSHIP, London, England, July 20-25, 1953. Mr. W. R. LeFanu, % London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, England, Chairman.

INTERNATIONAL CONGRESS OF MICROBIOLOGY, Rome, Italy, Sept. 6-12, 1953. For information write: Dr. V. Puntoni, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS OF MILITARY MEDICINE AND PHARMACY, Montevideo, Uruguay, March 1-7, 1953. Dirreccion General del Servico de Sanitad Militar, 8 de Octubre y Mariano Moreno, Montevideo, Uruguay, Secretariat of the Congress.

INTERNATIONAL CONGRESS OF OTORHINOLARYNGOLOGY, Amsterdam, Netherlands, June 8-15, 1953. Dr. W. H. Struben, J. J. Viottastraat 4, Amsterdam, Netherlands, Secretary.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Havana, Cuba, Oct. 12-17, 1953. Prof. Felix Hurtado, 5a Avenue 124, Miramar, Havana, Cuba, President.

INTERNATIONAL CONGRESS OF RADIO-BIOLOGY, Copenhagen, Denmark, July 14-25, 1953. Prof. Flemming Norgaard, Oster Voldgade 10, Copenhagen K, Denmark, Secretary General.

INTERNATIONAL CONGRESS OF RADIOLOGY, Copenhagen, Denmark, July 19-25, 1953. Professor Flemming Norgaard, 10 Oster Voldgade, Copenhagen K., Denmark, Secretary General.

INTERNATIONAL CONGRESS OF THALASSOTHERAPY, Dubrovnick, Yugoslavia, May 17-25, 1953. Prof. C. Plavaic, Mavrodne Republick 51, Belgrade, Yugoslavia, Secretary General.

INTERNATIONAL CONGRESSES OF TROPICAL MEDICINE AND MALARIA, Istanbul, Turkey, Aug. 28-Sept. 4, 1953. Professor Dr. Ihsan Sükrü Aksel, Tunel Meydam, Beyoglu, Istanbul, Turkey, General Secretary.

INTERNATIONAL FERTILITY ASSOCIATION, New York, N. Y., U. S. A., May 25-31, 1953. Dr. Abner I. Weisman, 1160 Fifth Avenue, New York 29, N. Y., U. S. A., Associate Secretary General.

INTERNATIONAL HOSPITAL CONGRESS, London, England, May 25-30, 1953. Capt. J. E. Stone, 10 Old Jewry, London, EC2, England, Hon. Secretary.

INTERNATIONAL LEPROSY CONGRESS, Madrid, Spain, Oct. 3-10, 1953. Dr. Felix Contreras, Moreto 15, Madrid, Spain, Secretary.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Montreal, Canada, Aug. 31-Sept. 4, 1953. Dr. A. S. V. Burgen, Dept. of Physiology, McGill University, Montreal, Canada, Secretary.

INTERNATIONAL STUDY CONFERENCE ON CHILD WELFARE, Bombay, India, Dec. 5-12. For information write: All India Save the Children Committee, 5 Carmichael Road, Bombay, India.

INTERNATIONAL UNION AGAINST CANCER AND INTERNATIONAL CANCER RESEARCH COMMISSION, Joint Meeting, Bombay, India. Dec. 28. Prof. Khanolkar, Tata Memorial Hospital, Bombay, India, President.

INTERNATIONAL VETERINARY CONGRESS, Stockholm, Sweden, Aug. 9-15, 1953. Prof. Axel Isaksson, Institute of Veterinary Medicine, Stockholm 50, Sweden, Secretary.

PAN AMERICAN CONGRESS OF THE MEDICAL PRESS, Buenos Aires, Argentine, July 12-16, 1953. Secretaria del Congress, 763 Uriburu, Buenos Aires, Argentine.

WORLD CONFERENCE ON MEDICAL EDUCATION, British Medical Association House, Tavistock Square, W.C.1, London, England, Aug. 24-29, 1953. Secretariat: World Medical Association, 2 East 103d St., New York 29, N. Y., U. S. A.

WORLD CONGRESS OF THE WORLD CONFEDERATION FOR PHYSICAL THERAPY, London, England, Sept. 7-12, 1953. Miss M. J. Neilson, Chartered Society of Physiotherapy, Tavistock House, South, Tavistock Square, London, W.C.1, England, Secretary.

DEATHS

Wright, Louis Tompkins ⊕ New York City; born in La Grange, Ga., July 23, 1891; Harvard Medical School, Boston, 1915; specialist certified by the American Board of Surgery; member of the American Trudeau Society; fellow of the American College of Surgeons and the New York Surgical Society; honorary fellow of the International College of Surgeons; founded the Harlem Surgical Society in 1937; chairman of the board of directors of the National Association for the Advancement of Colored People, and in 1940 recipient of its Spingarn medal in recognition of outstanding achievement by a Negro during the year; in 1917 commissioned a first lieutenant in the U. S. Army, and was awarded the Purple Heart during World War I; medical advisor to the New York City director of the Selective Service System; for many years police surgeon, police department of the City of New York; surgical director of the Harlem Hospital, where he was president of the medical board; director of the Harlem Hospital Cancer Research Foundation since 1948, when he founded the *Harlem Hospital Bulletin;* on the executive committee and advisory council, Department of Hospitals, City of New York; in 1938 received the honorary doctor of science degree from Clark University, Atlanta, Ga.; died Oct. 8, aged 61, of coronary thrombosis.

Neal, Paul Ardeen ⊕ Medical Director, U. S. Public Health Service, Bethesda, Md.; born in West Point, Tenn., June 25, 1901; Vanderbilt University School of Medicine, Nashville, 1927; entered the United States Public Health Service in 1928; from 1929 to 1933 was attached to the United States consulates in Germany, Italy, Denmark, Ireland, and Poland; from 1936 to 1947 was chief of industrial hygiene studies at the National Institutes of Health; served as head of the physical biology laboratories from 1947 to the present, directing medical research in such fields as molecular biophysics, nuclear radiation biology, and physiological physics; was assigned as chief of the laboratory of physical biology, National Institute of Arthritis and Metabolic Diseases; member of the American Public Health Association, American Association for the Advancement of Science, Washington Academy of Sciences, Association of Military Surgeons of the United States, American Industrial Hygiene Association, American Statistical Association, American Society of Human Genetics, and other organizations; recently directed field and laboratory research clarifying the effect of DDT on human beings; author of more than 100 scientific articles; died in Emergency Hospital, Washington, D. C., Oct. 13, aged 51, of coronary thrombosis.

Schloss, Oscar Menderson ⊕ Southold, N. Y.; born in Cincinnati, June 20, 1882; Johns Hopkins School of Medicine, Baltimore, 1905; emeritus professor of clinical pediatrics at Cornell University Medical College; at one time professor of pediatrics at Harvard Medical School in Boston; specialist certified by the American Board of Pediatrics; member of the American Pediatric Society, American Academy of Pediatrics, American Society for Serology and Hematology, Society for Experimental Biology and Medicine, and the American Society of Clinical Investigation consulting pediatrician at New York Hospital, Willard Parker Hospital, and New York Infirmary for Women and Children, all in New York; director of the children's service at New York Nursery and Childs Hospital in New York from 1923 to 1932; at one time medical director of the Infants' Hospital in Boston; died Oct. 6, aged 69, of coronary disease.

Copenhaver, Kyle Cornett ⊕ Knoxville, Tenn.; born in Marion, Va., June 20, 1886; Lincoln Memorial University Medical Department, Knoxville, 1912; member of the Southeastern Surgical Congress; fellow of the International College of Surgeons; past president of the Tennessee State Medical Association and the Knoxville Academy of Medicine; served overseas during World War I; district surgeon for the Louisville and Nashville Railroad and surgeon for the Southern Railway System; president of the Acuff Clinic; affiliated with Knoxville General Hospital and Fort Sanders Hospital, where he died Sept. 15, aged 66.

Fisher, Joseph William ⊕ Pittsburgh; born in Pittsburgh Nov. 8, 1881; Western Pennsylvania Medical College, Pittsburgh, 1903; assistant professor of radiology at his alma mater; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, Radiological Society of North America, and the American College of Radiology; past president of the Pennsylvania Radiological Society; served as vice-president of the Pittsburgh Radiological Society; affiliated with the Falk Clinic; roentgenologist, St. John's and Passavant hospitals; died Sept. 11, aged 70.

Marshall, William J. ⊕ Missoula, Mont.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1909; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the Pacific Coast Oto-Ophthalmological Society; fellow of the American College of Surgeons; served during World War I; formerly practiced in Polson, where he was mayor and president of the school board; affiliated with St. Patrick Hospital, where he died Sept. 23, aged 77, of coronary thrombosis.

Allen, David Kimball ⊕ Salt Lake City; Northwestern University Medical School, Chicago, 1914; served overseas during World War I; affiliated with Veterans Administration and Latter Day Saints hospitals; died Sept. 6, aged 72, of cerebral thrombosis.

Barron, William Martin, Rochester, N. Y.; Bellevue Hospital Medical College, New York, 1893; died Sept. 9, aged 82, of coronary heart disease.

Blitzsten, N. Lionel ⊕ Chicago; Rush Medical College, Chicago, 1916; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychoanalytic Association, American Psychiatric Association, and Central Neuropsychiatric Association; for many years on the faculty of Northwestern University Medical School, where he was an associate in the department of nervous and mental diseases; affiliated with Cook County and Cook County Psychopathic hospitals; died Sept. 27, aged 59, of chronic myocarditis.

Broeder, William Hugo ⊕ St. Louis; Washington University School of Medicine, St. Louis, 1923; died in St. Anthony's Hospital Sept. 26, aged 55, of cerebral hemorrhage.

Bucher, Robert Leon, Newtown, Pa.; Jefferson Medical College of Philadelphia, 1921; died in Jefferson Hospital, Philadelphia, Sept. 14, aged 57, of coronary insufficiency.

Buckley, Patrick H. J. ⊕ Buffalo; University of Buffalo School of Medicine, 1915; fellow of the American College of Surgeons; served during World War I; affiliated with Millard Fillmore Hospital, where he died Sept. 12, aged 61, of multiple myeloma.

Chaffee, Clay Center ⊕ Brunswick, Tenn.; Memphis (Tenn.) Hospital Medical College, 1913; died Sept. 4, aged 62, of progressive bulbar palsy and bronchopneumonia.

Creveling, Cyrus Robbins ⊕ Washington, D. C.; George Washington University School of Medicine, Washington, D. C., 1927; served during World War I; affiliated with Sibley and National Homeopathic hospitals; died Sept. 19, aged 54, of coronary thrombosis.

Crosson, Henry Joseph ⊕ Washington, D. C.; Georgetown University School of Medicine, Washington, 1890; an Associate Fellow of the American Medical Association; formerly member of the board of public welfare; on the staffs of Georgetown, Gallinger, and Providence hospitals; died Sept. 18, aged 82, of cerebral hemorrhage and hypertension.

⊕ Indicates Member of the American Medical Association.

Curry, John Milton ⊕ Donelson, Tenn.; Memphis (Tenn.) Hospital Medical College, 1907; affiliated with Jackson-Madison County General Hospital in Jackson and Tennessee Home Training School for Feebleminded Persons; died Sept. 21, aged 70.

Deal, Don West ⊕ Springfield, Ill.; Northwestern University Medical School, Chicago, 1904; an Associate Fellow of the American Medical Association; member of the Industrial Medical Association; member of the House of Delegates of the American Medical Association in 1917 and 1918; affiliated with St. John's Hospital and Memorial Hospital, where he died Sept. 13, aged 73, of myocardial infarction and diabetes mellitus.

Dowd, James Edward ⊕ Watsonville, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; member of the Utah State Medical Association; served on the staff of St. Mary's Hospital in Salt Lake City; died Sept. 8, aged 76, of coronary thrombosis.

Eckhardt, John Carl ⊕ Washington, D. C.; George Washington University School of Medicine, Washington, D. C., 1912; past president of the Washington Medical and Surgical Society; died in Sibley Memorial Hospital Sept. 1, aged 62, of cardiovascular renal disease.

Esserman, Arthur Losos ⊕ Denver; Washington University School of Medicine, St. Louis, 1922; specialist certified by the American Board of Pediatrics; clinical instructor in pediatrics at the University of Colorado School of Medicine; affiliated with Beth Israel, Children's, Colorado General, and National Jewish hospitals; died recently, aged 54.

Fehr, Harry John ⊕ Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1909; affiliated with St. Luke's Hospital and Children's Medical Center; died in Marlton, N. J., Sept. 15, aged 67, of cerebral thrombosis.

Foltz, J. Eliot ⊕ Hutchinson, Kan.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; fellow of the American College of Surgeons; affiliated with St. Elizabeth Mercy and Grace hospitals; died Aug. 20, aged 73, of cerebral hemorrhage.

Foulks, Wallace Scott, Coral Gables, Fla.; Jefferson Medical College of Philadelphia, 1897; died recently, aged 77, of arteriosclerosis, and cerebral hemorrhage.

Galloway, David, Memphis, Tenn.; Memphis Hospital Medical College, 1909; for many years staff member of the John Gaston Hospital; formerly superintendent of the Western State Hospital in Western State Hospital; died Sept. 6, aged 69, of hypertensive cardiovascular disease and arteriosclerosis.

Gaskin, Lewis Roy ⊕ Albemarle, N. C.; Medical College of the State of South Carolina, Charleston, 1921; member of the American Academy of General Practice; president of the medical staff of Stanly County Hospital, where he died June 9, aged 56, of coronary arteriosclerosis.

Gordin, Stanley Bernard ⊕ Alquina, Ind.; Indiana University School of Medicine, Indianapolis, 1930; died Sept. 1, aged 47.

Greenwood, Austin Ellsworth, Brooklyn; Tufts College Medical School, Boston, 1906; died Sept. 15, aged 70.

Grimes, Marvin, Hardin Mo.; Missouri Medical College, St. Louis, 1896; died in the Research Hospital, Kansas City, Mo., Sept. 7, aged 83.

Gunn, Neil Mackay, Michigan City, Ind.; Northwestern University Medical School, Chicago, 1911; died June 29, aged 69, of coronary sclerosis.

Habenicht, Mae Hall, La Jolla, Calif.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1899; died Sept. 1, aged 78, of heart disease.

Hailey, James Henry Jr., Bassfield, Miss.; Northwestern University Medical School, Chicago, 1950; interned at Mississippi Baptist Hospital in Jackson; died in Lutheran Hospital in Vicksburg Sept. 20, aged 33, of poliomyelitis.

Hawk, Mortimore C., Blue Island, Ill.; University of Pittsburgh School of Medicine, 1896; died Sept. 1, aged 79, of coronary thrombosis.

Higgins, Irving Wilber, Live Oak, Calif.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1904; died Sept. 7, aged 73, of coronary occlusion and arteriosclerosis.

Hoenig, Andrew Ladislaw, Cherokee, Iowa; University of Kolozsvár, Hungary, 1915; affiliated with Mental Health Institute; died Aug. 19, aged 61, of coronary occlusion.

Hooper, Joseph Ward ⊕ Wilmington, N. C.; University of Maryland School of Medicine, Baltimore, 1909; served overseas during World War I; past president of the New Hanover County Medical Society; formerly vice-president of the Tri-State Medical Association of the Carolinas and Virginia; consulting surgeon of the Atlantic Coast Line Railroad; a member of the board of directors of the Wilmington Savings and Trust Company; affiliated with Babies Hospital and James Walker Memorial Hospital, where he died Sept. 3, aged 65, of bilateral ureteral obstruction.

Hunter, Joseph William ⊕ Charleroi, Pa.; Jefferson Medical College of Philadelphia, 1893; affiliated with Charleroi-Monessen Hospital, where he died Aug. 24, aged 86, of arteriosclerosis and cerebral thrombosis.

Japha, Alfred Frederick, Denver; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1892; wounded while serving with the German Army during World War I and was awarded the Iron Cross; for 20 years medical director of the Kinderhaus in Berlin; author of "Handbook of Pediatrics"; chief of pediatrics at National Jewish Hospital, where he died Sept. 3, aged 81, of acute myocardial infarction.

Jenson, Conrad Heber ⊕ Ogden, Utah; Rush Medical College, Chicago, 1920; fellow of the American College of Surgeons; past president of the Utah State Medical Association and Weber County Medical Society; served on the staff of the Dee Hospital, where he died Sept. 2, aged 61, of acute lobar pneumonia and obliterative arteritis.

Jentgen, Leo George ⊕ Detroit; University of Michigan Medical School, Ann Arbor, 1919; fellow of the American College of Surgeons; on the staff of Providence Hospital; died in Bear Lake Aug. 10, aged 59, of a heart attack.

Jones, Elgin Wilbur ⊕ Wakefield, Mass.; University of the City of New York Medical Department, 1883; member of the American Academy of Ophthalmology and Otolaryngology and the New England Ophthalmological Society; affiliated with Lynn (Mass.) Hospital; died Aug. 22, aged 91, of cerebral hemorrhage.

Jurist, Charles ⊕ Springfield, Mass.; University and Bellevue Hospital Medical College, New York, 1914; member of the New England Pediatric Society; affiliated with Springfield Hospital; died Sept. 1, aged 61, of cancer.

Kennedy, John Alvin ⊕ Okmulgee, Okla. (licensed in Oklahoma by years of practice); died in City Hospital Sept. 12, aged 76, of carcinoma of the prostate.

Lederer, Max ⊕ Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1906; an Associate Fellow of the American Medical Association; specialist certified by the American Board of Pathology; formerly associate professor of pathology at Long Island College of Medicine; consulting pathologist at Rockaway Beach (N. Y.) Hospital, Jewish and Adelphi hospitals; discovered a blood disease known as Lederer's anemia; died Sept. 13, aged 67, of cerebral hemorrhage.

Lemon, Leon Bunyan, Cleveland; Starling-Ohio Medical College, Columbus, 1914; died Sept. 3, aged 60, of myocardial infarction.

Likely, David Stanley ⊕ New York; McGill University Faculty of Medicine, Montreal, Canada, 1905; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; consultant, New York City Hospital; died Sept. 11, aged 71, of carcinoma of the pancreas.

Lindeman, Howard Edward ⊕ New York; Columbia University College of Physicians and Surgeons, New York, 1906; consulting gynecologist, Hospital for Joint Diseases; died on a fishing boat just off Montauk Point, Long Island, Sept. 10, aged 69, of coronary occlusion.

Lojacono, Salvator Charles ⊕ Buffalo; University of Buffalo School of Medicine, 1917; served during World War I; formerly city fire department surgeon; died Sept. 7, aged 59, of myocardial infarction.

Lux, Paul ⊕ Kansas City, Mo.; University Medical College of Kansas City, Mo., 1905; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the American Laryngological, Rhinological and Otological Society; affiliated with Menorah and Kansas City General hospitals; died Sept. 20, aged 67, of coronary occlusion.

McBee, Kirby Smith ⊕ Owenton, Ky.; Louisville (Ky.) Medical College, 1898; served as vice-president of the Kentucky State Medical Association; died Sept. 18, aged 76.

McGowan, Michael J., Chicago; Baltimore Medical College, 1898; died Sept. 5, aged 82.

MacPhail, James Abram Garfield, Katonah, N. Y.; University and Bellevue Hospital Medical College, New York, 1903; affiliated with Northern Westchester Hospital in Mount Kisco; died in Mount Kisco, Sept. 11, aged 70, of arteriosclerotic heart disease.

Maloney, William J. M. A., New York; University of Edinburgh Faculty of Medicine, Edinburgh, Scotland, 1905; died in Edinburgh, Scotland, Sept. 3, aged 69, of fracture of the neck of the femur and pulmonary embolism.

Martin, Claude J., Hamtramck, Mich.; Maryland Medical College, Baltimore, 1911; affiliated with St. Francis Hospital, where he died Sept. 22, aged 66, of coronary occlusion.

Meggers, Edward Charles ⊕ Palo Alto, Calif.; University of Illinois College of Medicine, Chicago, 1917; owner of the McGregor Hospital in McGregor, Iowa, from 1924 to 1948; member of the Iowa State Medical Society; served during World War I; died in Palo Alto Hospital Sept. 5, aged 63, of hypertensive heart disease.

Middleton, Alonzo Bolen ⊕ Clermont, Fla.; Barnes Medical College, St. Louis, 1898; an Associate Fellow of the American Medical Association; member of the Illinois State Medical Society and the American Academy of Ophthalmology and Otolaryngology; served during World War I; affiliated with St. James Hospital in Pontiac, Ill., where he died Sept. 21, aged 76, of cerebral hemorrhage.

Miller, Harold Applegate, Augusta, Ga.; Western Pennsylvania Medical College, Pittsburgh, 1899; fellow of the American College of Surgeons, of which he had been one of the founders; at one time on the faculty of his alma mater; past president of the Allegheny County (Pa.) Medical Society and the Pittsburgh Academy of Medicine; formerly on the staff of Magee and Allegheny General hospitals in Pittsburgh; died in University Hospital Sept. 22, aged 78, of uremia.

Montefiore, Herbert Nathan ⊕ St. Albans, Vt.; University of Vermont College of Medicine, Burlington, 1898; affiliated with St. Albans and Kerbs Memorial hospitals; died Sept. 24, aged 79, of coronary thrombosis.

Moore, Benjamin Harrison ⊕ Oklahoma City, Okla.; Eclectic Medical College, Cincinnati, 1919; died Aug. 31, aged 62.

Morley, Francis Wayland ⊕ Toledo, Ohio; Cleveland-Pulte Medical College, 1911; member of the American Academy of General Practice; affiliated with Toledo, Mercy, and Flower hospitals; died Sept. 19, aged 66, of cerebral hemorrhage.

Nadler, Walter Herman ⊕ Chicago; Northwestern University Medical School, Chicago, 1913; associate professor of medicine at his alma mater; specialist certified by the American Board of Internal Medicine; member of the Central Society for Clinical Research, of which he had been president; fellow of the American College of Physicians; affiliated with Passavant Memorial and Wesley Memorial hospitals in Chicago and Veterans Administration Hospital in Hines, Ill.; died in Winnetka, Ill., Sept. 13, aged 63, of bronchogenic carcinoma.

Neuendorf, Frank Mathias, Wilmington, Del.; Albany (N. Y.) Medical College, 1911; died recently, aged 64, of coronary thrombosis.

Newman, Melvin Max ⊕ Chicago; University of Illinois College of Medicine, Chicago, 1924; died in South Chicago Hospital Sept. 6, aged 55, of coronary thrombosis.

Okerlin, Oscar William ⊕ Essex, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1905; died in Chariton Aug. 17, aged 79, of coronary thrombosis.

Ormsbee, James L. ⊕ Springfield, Mo.; Missouri Medical College, St. Louis, 1891; died July 9, aged 84, of arteriosclerosis.

Overton, Valdy Clinton, Houston, Texas; University of the South Medical Department, Sewanee, Tenn., 1898; died Sept. 12, aged 89, of cerebral vascular accident.

Owen, William Cornwallis ⊕ St. Louis; Missouri Medical College, St. Louis, 1889; died June 30, aged 86, of chronic myocarditis.

Parmenter, William Watts Jr., Struthers, Ohio; Western Reserve University School of Medicine, Cleveland, 1951; interned at Youngstown Hospital and died in the North Side Unit Sept. 12, aged 31, of ulcerative colitis and peritonitis.

Pay, Wilson Cyrus, DeLand, Fla.; University of Louisville (Ky.) Medical Department, 1894; died Aug. 12, aged 81, of coronary occlusion and rheumatoid arthritis.

Perkins, Raymond George ⊕ Malone, N. Y.; Syracuse University College of Medicine, 1911; fellow of the American College of Surgeons; affiliated with Alice Hyde Memorial Hospital, where he died Sept. 18, aged 68, of coronary occlusion.

Person, Edgar Cooper Jr. ⊕ New York; Cornell University Medical College, New York, 1935; associate professor of clinical surgery at his alma mater; member of the Society of University Surgeons and New York Surgical Society; fellow of the American College of Surgeons; affiliated with Bellevue Hospital and the New York Hospital, where he died Sept. 5, aged 42, of metastatic melanoma, originally of the left eye.

Phillips, Isaac Hildreth ⊕ Missouri Valley, Iowa; Ohio Medical University, Columbus, 1900; died July 28, aged 74, of angina pectoris and arteriosclerosis.

Porter, Miles Fuller Jr. ⊕ Fort Wayne, Ind.; Harvard Medical School, Boston, 1911; at one time on the faculty of Indiana University School of Medicine; formerly secretary and president of the Fort Wayne Medical Society; served during World War I; died Sept. 4, aged 65, of coronary thrombosis.

Powell, Alvin, Lafayette, Calif.; University of California Medical School, San Francisco, 1908; died Sept. 7, aged 69, of carcinoma.

Powell, Burke ⊕ Albia, Iowa; Marion-Sims College of Medicine, St. Louis, 1899; died Sept. 5, aged 77, of cerebral hemorrhage.

Pugsley, George William Jr. ⊕ North Platte, Neb.; University of Nebraska College of Medicine, Omaha, 1937; served during World War II; died Aug. 2, aged 40.

Rand, George Henry ⊕ Livermore Falls, Maine; Boston University School of Medicine, 1900; affiliated with Franklin County Memorial Hospital in Farmington and Central Maine General Hospital and St. Marys Hospital in Lewiston; died Aug. 3, aged 75, of arteriosclerosis.

Rariden, Lawrence Bradley, Greenfield, Ind.; Indiana University School of Medicine, Indianapolis, 1912; served during World War I; first president of the medical staff of Hancock County Memorial Hospital; for many years affiliated with Methodist Hospital in Indianapolis, where he died Aug. 26, aged 66.

Reeves, James Leroy ⊕ Hope Mills, N. C.; Temple University School of Medicine, Philadelphia, 1938; died in Brunswick, Ga., Aug. 11, aged 37, of injuries received in an automobile accident.

Reid, William E., Portsmouth, Va.; Leonard Medical School, Raleigh, 1900; died in Newport News, recently, aged 82, of acute myocarditis and nephritis.

Richter, Arthur Jacob ⊕ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; an Associate Fellow of the American Medical Association; died in Michael Reese Hospital Oct. 2, aged 75.

Rischin, Meer, Brooklyn; Universität Bern Medizinische Fakultät, Switzerland, 1918; affiliated with Adelphi, Unity, Jewish, and Israel Zion hospitals; died July 29, aged 65, of carcinoma of the bladder.

Rockey, Paul ⊕ Portland, Ore.; Columbia University College of Physicians and Surgeons, New York, 1908; member of the founders group of the American Board of Surgery; member of the Pacific Coast Surgical Association and the North Pacific Surgical Association; fellow of the American College of Surgeons; past president of the Multnomah County Medical Society; surgeon, Good Samaritan Hospital; consulting surgeon, Doernbecher Memorial Hospital for Children and Multnomah Hospital; died Sept. 6, aged 68, of cerebral hemorrhage.

Rogers, Olin Welbourne ⊕ Knoxville, Tenn.; University of Nashville Medical Department, 1910; died in Daytona Beach, Fla., July 31, aged 68, of mesenteric thrombosis and arteriosclerosis.

Rosecrans, James Hankinson ⊕ Hoboken, N. J.; Bellevue Hospital Medical College, New York, 1883; an Associate Fellow of the American Medical Association; died in Secaucus, Sept. 5, aged 95.

Royster, Thomas Hays, Tarboro, N. C.; University College of Medicine, Richmond, 1908; died in Edgecombe General Hospital July 3, aged 67, of coronary thrombosis.

Rumrill, Samuel Dudley ⊕ St. Petersburg, Fla.; University of Vermont College of Medicine, Burlington, 1903; member of the Massachusetts Medical Society; died July 1, aged 76, of coronary thrombosis.

Ryan, Jerome Joseph ⊕ Providence, R. I.; McGill University Faculty of Medicine, Montreal, Canada, 1933; died in South Harwich, Mass., recently, aged 47, of coronary occlusion.

Saeltzer, Dudley Victor Jr. ⊕ Sacramento, Calif.; University of California Medical School, San Francisco, 1931; specialist certified by the American Board of Surgery; served during World War II; died Sept. 12, aged 45.

Sarason, Peter Benjamin, Miami Beach, Fla.; Johns Hopkins University School of Medicine, Baltimore, 1912; died July 1, aged 64, of coronary thrombosis and arteriosclerosis.

Scarborough, Alfred Jr., New York; Medical College of the State of South Carolina, Charleston, 1952; intern, Roosevelt Hospital; died Sept. 15, aged 25.

Scurlock, Herbert Clay, Washington, D. C.; Howard University College of Medicine, Washington, 1900; professor of physiochemistry, emeritus, at his alma mater; died in Emergency Hospital Sept. 27, aged 77, of uremia and nephritis.

Shaffer, Earl William ⊕ Chicago; Rush Medical College, Chicago, 1922; specialist certified by the American Board of Internal Medicine; affiliated with Ravenswood Hospital, where he died Sept. 2, aged 58, of cerebral hemorrhage.

Shine, Dan William ⊕ Oelwein, Iowa; State University of Iowa College of Medicine, Iowa City, 1914; served during World War I; died Aug. 18, aged 67, of bronchiectasis and myocardial insufficiency.

Shinnick, John Dill, Spokane, Wash.; Rush Medical College, Chicago, 1903; formerly member of the Idaho state legislature; served during World War I; died Sept. 2, aged 76, of arteriosclerotic heart disease.

Shuman, George Hull, Pittsburgh; Medico-Chirurgical College of Philadelphia, 1910; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; served as president of the Pittsburgh Ophthalmological Society; affiliated with Western Pennsylvania Hospital, where he died Sept. 3, aged 68, of bronchopneumonia.

Sigrest, Otho Randolph ⊕ Gadsden, Ala.; Birmingham Medical College, 1908; died recently, aged 74, of tuberculosis of the liver.

Skiff, Francis Sands ⊕ Fort Lauderdale, Fla.; University of the City of New York Medical Department, New York, 1888; died recently, aged 85, of carcinoma of the pancreas.

Small, Arthur Atwell ⊕ Asheville, N. C.; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1895; member of the Illinois State Medical Society; formerly practiced in Chicago, where he was on the faculty of Rush Medical College, on the staff of St. Joseph's Hospital, and medical director of the Chicago Surface Lines; died in Wesley Memorial Hospital, Chicago, Aug. 18, aged 79, of carcinoma of the liver, spleen, kidneys, and colon.

Statzer, J. C., Bristol, Tenn. (licensed in Tennessee in 1909); died Aug. 25, aged 76, of cerebral hemorrhage.

Steen, Harry M. ⊕ Springfield, Ill.; Indiana University School of Medicine, Indianapolis, 1931; specialist certified by the American Board of Pathology; member of the College of American Pathologists and the American Society of Clinical Pathologists; affiliated with St. John's Hospital; died Sept. 5, aged 47, of a skull fracture received in a fall.

Steenbergen, John Harness ⊕ Huntington, W. Va.; College of Physicians and Surgeons, Baltimore, 1908; died Aug. 27, aged 68.

Steinbach, Henry Frank, Chicago; Northwestern University Medical School, Chicago, 1933; served during World War II; died in Veterans Administration Hospital, Hines, Ill., Aug. 29, aged 45, of cardiac infarction.

Stelle, Harry Lewis, Pittsburg, Kan.; Beaumont Hospital Medical College, St. Louis, 1896; on the staff of Mount Carmel Hospital, where he died Aug. 30, aged 80, of cancer.

Stevens, George Albert, Stockton Springs, Maine; Bellevue Hospital Medical College, New York, 1888; died recently, aged 88, of arteriosclerosis.

Stevenson, Olen Jay, Chester, Pa.; Baltimore Medical College, 1906; died Aug. 21, aged 69.

Surratt, Reuben B., Porter, Okla.; Meharry Medical College, Nashville, Tenn., 1905; died Aug. 20, aged 75, of a heart attack.

Torgerson, William B. ⊕ Oklee, Minn.; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1897; member and treasurer of the local school board; served on the staff of St. Luke's Hospital in Thief River; died July 7, aged 80.

Walvoord, William W., Dunlap, Iowa; University of Nebraska College of Medicine, Omaha, 1916; died Aug. 22, aged 61, of cerebral hemorrhage.

Watkins, David Alexander ⊕ Buckhannon, W. Va.; Rush Medical College, Chicago, 1929; served during World War II; affiliated with Veterans Administration Hospital in Clarksburg; died in Philippi Sept. 26, aged 50, of coronary occlusion.

Weaver, Cleo Earl, La Belle, Fla.; Indiana University School of Medicine, Indianapolis, 1908; died in Lee Memorial Hospital, Fort Myers, July 18, aged 71, of carcinoma of the throat.

Wehrly, John ⊕ Santa Ana, Calif.; Missouri Medical College, St. Louis, 1890; member of the Radiological Society of North America; past secretary and president of the Orange County Medical Society; past president of the Orange County Tuberculosis Society; formerly county health officer; served during World War I; died in St. Joseph Hospital Aug. 14, aged 84, of subdural hematoma.

Weirauk, Herbert Vance, Columbus, Ohio; Western Reserve University School of Medicine, Cleveland, 1915; specialist certified by the American Board of Radiology; member of the Radiological Society of North America; fellow of the American College of Physicians; served during World War I; affiliated with White Cross Hospital; died Sept. 1, aged 64, of a heart attack.

Wulf, William Frederick, Miami, Fla.; Chicago Medical School, 1917; died in Jackson Memorial Hospital recently, aged 73, of arteriosclerosis.

Zimmermann, Ernest Ludwig, Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1916; died in Johns Hopkins Hospital recently, aged 61, of cerebral thrombosis and arteriosclerosis.

FOREIGN LETTERS

COLOMBIA

Bartonellosis.—Dr. Luis Patiño Camargo, professor of clinical medicine on tropical diseases, in the Faculty of Medicine of the National University, wrote an article on "Verrucose Fever of Guaitara in Colombia," which was published in the *Revista de la Facultad de Medicina of Bogota* in June, 1952. Verrucose fever of Guaitara, which is a form of bartonellosis, Carrion's disease, or Peruvian wart, was discovered in 1939 by Patiño Camargo, who made a clinical diagnosis in patients with fever and warts in the Sandoná Hospital. Sandoná is a town in the south of Colombia. The diagnosis was confirmed by the finding of Bartonella in the blood of a patient who was in the early febrile stage of the infection. Since 1936, the disease, in an epidemic form and with a high mortality, has disturbed the medical profession and the public. The disease had apparently passed unobserved for many years in the lowlands of the Andean regions and in the chains of Colombian mountains. The conditions for spread of this disease are similar to those observed with the disease "Sirki quechua" of the Peruvian Mountains. The disease first spread into rural regions and towns of the southern territories of Colombia with a mild climate. Deaths in Bogotá and Cali have been reported, but the patients had contracted the disease in the Nariño Department. In Latin America, there are three definite loci of bartonellosis in human beings, namely, Perú, Ecuador, and Colombia. The disease affects an area from a northern latitude of 2 degrees to a southern latitude of 13 degrees. In the 1936 epidemic in Colombia, the disease was highly virulent. The highest incidence was in adult peasants; however, cases were found in both sexes, regardless of age and living conditions. The greatest incidence was among persons living in rural zones, but there were several cases in cities. There were about 1,800 deaths in the period from January to September, 1938. In five municipalities there were 1,937 deaths from the disease during 1939 and 1940, and in 41 municipalities of the Nariño Department there were 646 deaths in 1941. The total number of deaths from the disease is above 6,000. According to Dr. Patiño Camargo, the cause of verrucose fever of Guaitara is Bartonella bacilloformis, which was found in blood of patients in the epidemic in the southern territories of Colombia. It proved to be the same Bartonella described by Alberto Barton in 1905. Dr. Patiño Camargo, in his 1939 report, stated that lice was one of the transmitting agents and that there may be other agents, as in the case in the transmission of Rickettsia. Definite identification of the transmitting agents has not as yet been reported.

Anemia is the predominant condition in the early period of the disease, whereas warts are predominant in the last period. The author reported the results of his experiments on 97 animals that had been inoculated with strains of Bartonella. He also reported the results of studies on postmortem material from human bodies and biopsies on patients observed in hospitals. Also reported were the results of six studies on experimental wart in Macaca rhesus and Cebus fatuellus. In these experiments, the author was assisted by Dr. M. Sánchez Herrera, pathologist of the Hospital in San Juan de Dios of Bogotá. In his report to the authorities in Colombia in January, 1939, he recommended steps for prevention of the disease. The disease has lost the acute character it had formerly, and it also has lost its epidemic character.

Personal Items.—Dr. Robert R. Williams, of the United States, discoverer of thiamine, was in Bogotá during the week of Sept. 7 to 14, 1952. Dr. Williams is visiting Latin American countries for the State Department of the United States. He is collaborating with the government in campaigns for improving nutrition.

Dr. George T. Pack of the Memorial Hospital in New York was invited to the Congress of Medicine recently held in Guayaquil, Ecuador. He then visited Bogotá from Sept. 10 to 22, 1952, in response to a special invitation of the Consultorio de Especialistas Society. He lectured before this group and others on "Melanoma and Malignant Tumors of Soft Tissues" and "Recent Progress on Treatment of Cancer." He performed on patients in the Institute of Radium and in the San Juan de Dios hospital in Bogotá.

ECUADOR

Social Security.—Until 1937 social security in Ecuador covered only fiscal employees, the military, the police, and municipal employees; but in that year the law of obligatory social security was passed, thereby putting the majority of employees and workers theoretically under the protection of social security. In practice, however, social security has, as yet, not extended to the agricultural workers but only to the workers and employees in the cities. Social security includes some important provisions such as care in illness, maternity, old age, invalidism, and occupational accidents. In addition it extends short term credit of an amount that rarely exceeds three times the salary and provides 30 year mortgages for those buying a home. Moreover, social security has undertaken, in the majority of cities in the republic, extensive building programs to provide adequate housing at low cost. Workers and employees pay 5% of their salaries, of which 2% covers health insurance. The employers at present pay 6%, but should pay 7%, on the salaries of all their employees and workers; moreover, for the pensioning of their workers they pay one month's salary each year. The public and municipal employees pay 7% (including death benefits), and the state contributes 7%.

The most important part of social security is undoubtedly the medical department. Although theoretically the medical department is in charge of preventive medicine, in reality its work and the available funds are used exclusively for medical aid. The organization utilizes local clinical hospitals in the most important cities and an ample network of dispensaries. All medical assistance of the insured is in charge of the social security organization: medical service, drugs, surgical service, hospitalization, and maternity service. Furthermore, social security during the time of hospitalization or while the worker is incapacitated pays 75% of the salary of the worker. Social security also pays 75% of the salary of pregnant women for two weeks before delivery and four weeks after delivery. Recently under a special regulation the medical department has begun to offer certain medical services at a very low charge to close relatives of the insured, such as children, wife, and parents. Thus, progressively and silently, socialization has embraced the medical services of this country to a considerable extent. From the viewpoint of the worker and the employed person, social security represents an interesting institution: he can have medical services that he needs as soon as he needs it either in his home, in the dispensary, or in hospital clinics. He also has a prospect of acquiring his own house, retiring, and seeing to it that his children or his wife, in case of his death, will receive a small pension.

Nevertheless, the insured is not always satisfied with the medical service. The medical department has its own medical personnel, physicians, nurses, and other auxiliary medical workers, and the insured cannot choose his own physician or the best known specialist. The medical department has its own drug stores in which it is not possible to buy the thousands of necessary or unnecessary drugs that can be purchased in the ordinary drug store. The insured person often believes that the social security selects only drugs that are the cheapest, and for this reason he is very dissatisfied. Moreover, in special cases he likes to obtain consultation of some other physician.

From the point of view of social service the medical department of social security has made a successful experiment and it is solidly established and seeks to extend itself to the rural regions; however, the establishment of social security has pro-

The items in these letters are contributed by regular correspondents in the various foreign countries.

duced a serious problem for the physicians, which becomes more acute every day. The consulting rooms of the physicians in the large urban centers, with rare exceptions, are almost empty. It is difficult for a physician to subsist in a city without some employment in this social security or in some hospital, and in general the salaries are low.

On the other hand, the hygienic and sanitary conditions of the rural regions are very backward and the physician does not readily decide to practice in the country. These are some of the reasons why there is a relatively large number of physicians in the two large cities, Quito and Guayaquil, in which there is approximately one physician for every 1,000 inhabitants, whereas in the rural regions there is hardly one physician for 10,000 inhabitants

Fourth National Medical Congress.—On Sept. 17 the Fourth Medical Congress will assemble. The official subjects will be discussed by the following speakers: clinical forms of hepatic insufficiency observed in the three regions of the country, Dr. Armando Pareja Coronel; clinical aspects and various forms of allergy, Dr. Plutarco Naranjo; surgery of the prostate, Dr. Teodoro Maldonado Carbo; and surgery of the biliary passages, Dr. Dionisio Espinoza Vega. There will be a symposium on cancer as a medicosocial problem. The speakers will be Drs. Juan Tanca Marengo and Eduardo Ortega.

ITALY

Laurence-Moon-Biedl's Syndrome.—At a meeting of the medical and surgical society of the Romagna region, of which Professor De Castro is chairman, Dr. Gobbi reported the occurrence of Laurence-Moon-Biedl's syndrome with retinitis pigmentosa, adiposogenital dystrophy, polydactylism, syndactylism, and mental deficiency in two brothers. The two cases were compared with a case of Frohlich's syndrome secondary to fetal meningoencephalitis that could have been erroneously classified as a form of Laurence-Moon-Biedl's syndrome.

In the discussion that followed, Professor Battistini agreed that the clinical picture of these cases justified their classification as examples of Laurence-Moon-Biedl's syndrome. In fact, the presence of syndactylism and hexadactylism is sufficient to justify the congenital heredodegenerative character of the disease in the two patients who were members of the same family. This disease is linked to anatomic and functional alterations of the diencephalohypophyseal region, as is demonstrated in patients with Laurence-Moon-Biedl's syndrome in whom syndactylism is not present but in whom histological examination reveals small cell infiltrations of the paracentral lobules. In these patients the radiological examination of the cranium sometimes reveals sellar and suprasellar alterations.

Functional Syndromes After Gastric Resection.—At a meeting of the Neapolitan Society of Surgery Dr. D. Rodinó discussed the development of gastrojejunal functional syndromes secondary to gastric resection and their treatment. After a gastric resection various gastrojejunal functional syndromes may occur owing to a small stomach, abrupt evacuation, stasis in the afferent loop, or hypoglycemia. These syndromes are due especially to atony of the gastric stump and the anastomosed jejunal loop. In most cases the syndromes are not severe and can be cured with proper medical therapy, consisting mainly of a proper dietetic and hygienic regimen and administration of preparations that stimulate intestinal peristalsis. In some cases anesthetic infiltrations of the right splanchnic nerve are useful, in that they stimulate the vagus and a greater tonus and better motility of the anastomosed area are obtained. With this method Dr. Rodinó obtained the disappearance or the attenuation of the disturbances in some patients. When, despite the therapy adopted, the syndrome persists, it generally indicates a severe dysfunction of the gastrojejunal area or the existence of a concomitant organic factor. In these cases, which are, however, very rare, recovery may be obtained with surgical intervention. Two of his patients recovered.

In the discussion that followed, Professor Cantelmo reported that he obtained good results with continuous suction in one patient who, after gastric resection, had early disturbances of evacuation owing to edema of the neostomy. Professor Perrotti reported that he found only rare cases of gastrojejunal functional syndromes after common resections for gastric ulcers. He observed them with great frequency, however, in cases of resection for a peptic ulcer secondary to anastomosis when, for mechanical reasons, he was compelled to follow the antecolic way instead of the transmesocolic way. With the antecolic way a long loop is necessary, while the afferent loop is diminished by the presence of an end-to-end anastomosis. The speaker believes that the refilling of the afferent loop causes autonomic reflexes that reveal themselves with the dumping syndrome. In his cases the manifestations were transitory and were cured with medical therapy, proper diet, and lying on the back after the meals.

Meat in the Diet.—During a national convention on nutrition held in Bologna, Prof. Dario Jasonni reported on problems in the production of meat and pointed out the progress that has been reached in scientific studies of the human diet. After considering the biological value of vegetable and animal proteins, the speaker said that it is necessary that 40 to 50% of the total amount of proteins in the diet be animal proteins. Having pointed out that there is no scientific basis for complete vegetarianism, the speaker discussed the advantages of meat as compared with foods of vegetable origin because of its greater protein content and its abundance of iron. Considering the minimum physiological amount of proteins necessary for the human organism, the speaker concluded that the daily intake of proteins should be 120 gm., which means administration of 150 gm. of meat every day. In comparing the optimal dose of vegetable and animal proteins with those of the usual diet of Italians, Professor Jasonni pointed out the great deficiency of the average diet of the Italians in which, according to De Marzi's statistics, the daily intake of animal proteins is 20 gm.

LONDON

Meeting of the B. M. A.—At a recent meeting, the British Medical Association, studying medicopolitical problems, recommended that a general practitioner in the National Health Service should be penalized only for an infraction of his terms of service as stated in the National Health Service Act and not for an offense against the so-called spirit of the act. Under the regulations a physician could be penalized for conduct that could bring discredit on the health service. An attempt is being made to improve the terms and conditions of the service and to make them fair to the public and the physicians. At the moment they are not so fair as they might be, for a physician could be taken off the service when no breach of the terms of service has been proved against him. A suggestion was made that hospitals should give sealed notes to patients, containing details of diagnosis and treatment, to take to their own physicians on leaving hospital, but it was argued that some patients, in the past, had steamed open such letters, causing irreparable harm to the patient and also to the physician. Strong protest against the Ministry of Health requirement that hospital consultants retire at 65 brought forth a resolution that was adopted. It stated that this condition was contrary to the national policy that persons over 65 remain at work as long as they continued to carry out their duties efficiently. It was argued that general practitioners are allowed to work when they are over 65 although consultants are not given the same privilege.

Infectious Diseases.—A warning that in 20 years there will be panic in Britain, unless some positive action is taken now to make the importance of vaccination and inoculation widely known, was expressed. In these days of high speed travel there is a very grave risk of epidemics, particularly of smallpox, spreading in Britain. The Ministry of Health is accused of complacency in regard to the inadequacy of propaganda about infectious disease.

Hobbies.—An innovation at these meetings was an exhibition of physicians' hobbies. They ranged from handwoven clothes to boats. Among physicians are found collectors, artists, and writers, but the majority appeared to get the most enjoyment out of making things. A set of powder puffs and a specimen of

carpet all made from bulrushes were shown, and also a woman's coat and a boy's overcoat woven at home from Cheviot tweed were presented.

Pulmonary Embolism.—The *British Medical Journal* of July 5, 1952, in its lead article calls attention to pulmonary embolism in relation to the hazards of anticoagulant therapy and the problems of vein ligation and postulates whether either of these measures has yet justified widespread practice. Some authorities in the United States and Scandinavia have presented a somewhat confusing picture of the dangers of pulmonary embolism and the merits of anticoagulant therapy, but it is certainly true to say that nonfatal pulmonary embolism is still all too often overlooked, both clinicians and radiologists tending to suggest other diagnoses when the true state of affairs should be recognized. Although Cutler and Hunt in 1922 suggested that more than 50% of postoperative pulmonary complications were embolic in nature, surgeons have been slow to appreciate the frequency of this condition and physicians have only lately recognized how common thromboembolism is. It has been pointed out that pulmonary embolism occurred more commonly than any other serious acute pulmonary disease in a general hospital. In radiological diagnosis the shadows of pulmonary infarcts are commonly attributed to pulmonary collapse, consolidation, or raised diaphragm.

In considering the site and origin of thrombosis, Bauer suggested that the thrombosis that precedes pulmonary embolism starts usually in the muscular tributaries of the calf, and this is the generally accepted opinion. Boyd, however, takes a rather different view and contends that thrombosis more often begins in the femoral vein at the level of the adductor opening. In support of this theory, the absence of preceding signs in the calf in from 50% to 80% of patients with pulmonary embolism is noted but may equally well be due to the fact that tenderness in the calves occurs only after the thrombi are organized, whereas the potential embolus is rapidly built up before such organization has had time to occur. Also, it is usual to note etiological factors such as vein damage, venous stasis, and blood changes. Venous stasis can be counteracted by active movements, but, whereas leg thrombosis is probably reduced by this practice, it has not been proved that pulmonary embolism is substantially diminished.

The question of prophylactic anticoagulant therapy is constantly under review, but the published figures are not highly impressive. This therapy is largely out of the question in surgical practice, but since the surgical patient is particularly liable to thromboembolic complications when he first gets up, Short suggests that anticoagulants might well be given at this stage, when the risk is greater than usual, as, for example, after prostatectomy. Surgeons, on the other hand, recognizing the risk of bleeding in these cases, tend to avoid such treatment; for experience has shown that its dangers can be greater than those of the disease itself. Also it has been pointed out that any system of selective prophylaxis would cost approximately $5,000 for every death averted and $22 for every patient treated. While treatment with bishydroxycoumarin (dicumarol®) and the newer anticoagulants is cheaper, the trouble and risks of such a regimen would seem to neutralize most of its possible benefits.

Experiments in vein ligation in the hands of different workers seem to give rise to contrary conclusions, and among the measures advocated for the treatment of established pulmonary embolism, the administration of heparin has been successful with some but not with others. Others are equally indecisive. Although modern methods of treatment have tended to promote an enthusiasm in some clinicians that is matched only by the skepticism of others, it would be fair to say that each of the methods discussed is capable of making some positive contribution to the solution of this difficult problem.

Uterus and Gallbladder.—Louros and Kaïris call attention in the *British Medical Journal* (p. 20 [July 5] 1952) to the frequency with which hepatocholecystopathy coexists with menstrual disorders. In a great number of cases they contend that retrodisplacement, by pressing on the bowel, may cause symptomatic chronic constipation, which can lead to indigestion and hepatocholecystopathy, thus affecting the normal excretion of estrogens and consequently resulting in menstrual disorders. It is common knowledge that frequently retroversion is associated with menstrual irregularities, many of which become corrected or alleviated if anteversion is achieved. The latter physical state, to be permanent, can only be assured by the operation of ventrofixation, and this is to be preferred to correction by appliance. If ventrofixation does not bring about the required menstrual relief, a further proportion of cases can be assisted by the judicious use of endocrines. At the same time, the authors point out that retrodisplacement, when known to be present, does not necessarily cause backache, lower abdominal pains, and menstrual disorders; however, the two syndromes seem to be sufficiently commonly associated to make it well worth while finding out if the uterus is backwardly displaced and, if it is, to perform ventrofixation with a reasonable hope that the signs and symptoms of either syndrome may be relieved, sometimes the one more so than the other. There is then a chance that estrogens will be more successful.

Horse Shoe Club.—Some details concerning the Horse Shoe Club for encouraging Anglo-American cooperation, particularly among physicians, have already been given in THE JOURNAL (**148:**570 [Feb. 16] 1952). At the annual general meeting of the club, which was held recently under the chairmanship of Dr. Geoffrey Bourne, it was reported that an American section of the club has been formed and already has 150 members. Details were also given of the scheme organized by the club, whereby American Air Force medical officers who had been given a week's study leave in London were shown around the London hospitals and introduced to consultants in their specialty. Col. R. Braswell of the U. S. Air Force, who was present at the meeting, expressed his appreciation of the plan and hoped that it might be repeated this year. It was announced that it would certainly be continued. The club subserves a most useful function in providing help to visiting American physicians by putting them in touch with those aspects of medical activity in which they are interested. The secretary (Dr. Claude Nicol, St. Bartholomew's Hospital, London, E.C.1) will welcome inquiries from any American physician who is planning on visiting in Great Britain and would like assistance in such matters.

Joint Meeting of Orthopedic Associations.—According to the *British Medical Journal* Queen Elizabeth the Queen Mother attended the inaugural ceremony of the first Joint Meeting of Orthopaedic Associations of the English-Speaking World on June 30. The Queen Mother and presidents and members of the various orthopedic associations were welcomed by the Chancellor of London University, the Earl of Athlone, who was accompanied by the Countess of Athlone. The earl is the great-uncle of Queen Elizabeth II. The Queen Mother addressed the meeting and then presented jewels of office to the presidents of visiting orthopedic associations, who included Dr. Fremont A. Chandler (United States) and Dr. R. Graham Huckell (Canada). Lord Woolton, Lord President of the Council, welcomed the members of the conference on behalf of the government, and Sir Reginald Watson-Jones, president of the British Orthopaedic Association, also spoke.

Royal Society of Medicine.—The Royal Society of Medicine has enjoyed a visit from Dr. M. N. Smith-Petersen of Boston, and the president, Lord Webb-Johnson, conferred on him its diploma of Honorary Fellowship. Dr. Smith-Petersen then read a paper entitled "Lessons Learned from 14 Years' Experience with Mould Arthroplasty of the Hip-Joint." He recalled that the purpose of an arthroplasty was to relieve pain and restore the greatest possible function to the joint, and the essence of the operation is the insertion of a smooth surfaced mold of inert metal between the refashioned head of femur and acetabulum. He had performed 1,039 arthroplasties, with only 1 operative death. Wound infection had occurred in 42 cases, but improved methods of anaesthesia, transfusion during operation, and antibiotics had helped to make the operation safe even for old patients.

The Closed Shop.—An article in the *British Medical Journal* reports that the end of the Durham Closed Shop dispute seems to be in sight. At the invitation of the Minister of Labor, representatives of the Durham County Council and the Joint Emer-

gency Committee of the Professions have met and asked the minister to appoint a board of arbitration, whose findings both sides agree to accept. The "professions" concerned include physicians, dentists, professional engineers, midwives, nurses, and teachers, and they maintain that they should not be required to belong to a trade union or professional organization. As a step toward final agreement, the teachers have agreed to withdraw their notices of resignation, and the county council has decided to suspend the operation of the regulation that gave rise to the dispute.

Hospital Administration.—A member of the House of Commons reported the number of persons concerned solely with administration (excluding porters, engineers, and cooks) in a hospital management group, controlling 1,500 beds, to be 176 full-time workers and 8 part-time workers.

PARIS

Disease of the Diencephalon and Psoriasis.—The pathogenesis of psoriasis has long been the subject of research in France. Margarot, Bolgert, Poisson, and Soulié considered it a psychodermatosis, while Professor Charpy of the Marseilles school thought it to be an adaptation syndrome. Even many patients believed the origin of their disease to be emotional, but this remained to be proved. Fabre, Pitot, and Mrs. Pitot-Muzard have attempted to clear up this obscure pathogenesis without any tangible evidence. The authors thought that these causes, to be taken into account, must have acted in predisposed environments due to perturbation of receptive centers. The existence of a stress is conditioned by two factors: the aggression and the organism reacting to it, without which there is no syndrome. According to Camus and Roussy's works and those of Margarot, the authors have been looking for the reception of the aggression into the diencephalon and hypothalamus areas normally regulating the affective life. Their first investigations, results of which were reported to the Lyons Society for Dermatology and Syphilography, were made, among other dermatoses, on eight patients with psoriasis who were studied by means of psychosomatic examinations, particularly with electroencephalograms. The latter produced graphs generally characterized by desynchronization and an excessive drive by the slow and, sometimes, by rapid thalamic rhythms. Some of these can be superposed to those of patients with diencephalic lesions. The authors believe that electroencephalograms may procure useful information not only in psoriasis but also in other dermatoses, as the organism may react to a similar aggression by different cutaneous manifestations such as bullous dermatitis of the Duhring type, eczema, prurigo, or others. Fabre and his associates do not think that all these dermatoses are psychodermatoses. The choice of the therapy would depend on the nosological diagnosis, which might explain the difference in results obtained with hypophysial and adrenocortical treatments even of corticotropin (ACTH) and cortisone. Fabre and his associates stated that other cases, still under study, confirm the first results of their investigations, which they are pursuing in psoriasis and other dermatoses; they also insisted on the necessity of investigations performed on a large scale and pursued in close collaboration by dermatologists and psychiatrists, as recommended by Professor Gaté (Lyons).

International Meeting of Neurologists.—The French Society for Neurology had not resumed its international meetings since the war. The recent meeting, July 7-10 at the Salpétrière Hospital, coincided with the commemoration of the centenary of Prof. Pierre Marie. The topic of discussion was the question of involuntary and abnormal movements. E. Krebs delivered a lecture on the symptomatology of myoclonia, J. Lefebvre and J. Scherrer on electromyography in the study of abnormal movements, and H. Gastaut and A. Remond on electroencephalographic studies of myoclonia based on 1,500 cases. M. David, H. Hécaen, and J. Talairach spoke on surgical treatment of abnormal movements by section at the level of the lenticular fasciculus and specially of the ansa lenticularis. They described three techniques: (1) the subfrontal route (not recommended), (2) the transtemporal lateral route, and (3) the transfrontal route. Fénélon operated on 11 Parkinson's syndromes without any fatal results. The results were: one failure, two transient improvements, and eight (72%) satisfactory results, among which one dating back to 2 years and another to 18 months. The author thinks that persons to be operated on ought to be carefully selected and that the forms of unilateral Parkinson's disease with predominance of tremor are those for which operation is best indicated.

In a "deviational study in the course of temporal crisis," C. Castels (Montevideo), H. Gastaut, R. Vigouroux, and S. Ferrer (Santiago de Chile) report the data obtained in 15 temporal epileptic patients, in whom they studied the phenomena of deviation obtained by chemical activation. The authors divided the observed movements into three categories, each having a particular physiopathological significance: (1) tonic involuntary deviations, usually contralateral, less characteristic than and slightly preceding the generalization of the crisis; (2) the involuntary contralateral deviations of gesture, more characteristic of temporal epilepsy and often of great value for the localization of the affection; and (3) the gesture reaction, not involuntary, producing rotation to an ipsilateral or contralateral side, which is not an expression of a positive manifestation of the temporal crisis but a negative phenomenon related to a fall in the level of consciousness. H. Gastaut and H. Terzian (Padua) delivered a lecture, based on the study of 250 psychomotor crises, provoked by an intravenous injection of pentylenetetrazol (cardiazol®) in temporal epileptic patients, on "correlation between automatism of temporal crisis and the accompanying electrographic phenomena."

Cortisone in Painful and Ankylotic Periarthritis of Shoulder.—The treatment of this disease by the classical methods is long, exhausting, and very expensive. Prof. S. de Sèze and Drs. J. Robin and N. Debeyre, who have been using cortisone at the Lariboisière Hospital, reported their results in 15 cases at a recent meeting of the Medical Society of the Paris Hospitals. As a rule, to obtain satisfactory results a drastic treatment is necessary: 200 mg. on the first day, then 100 mg. daily for at least 10 to 12 days, from the 12th day, 100 mg. twice every third day, and then 50 mg. twice every other day. The total dose is about 1,500 mg. In the case of a physician, the treatment, which had been discontinued on the fourth day after an apparently complete recovery, was immediately followed by a relapse. The striking feature of this treatment is the almost immediate alleviation of pain. Patients depressed by pain and insomnia experience euphoria, and on the sixth or seventh day their general condition is transformed for the better. Of the 15 cases, the authors noted 11 complete recoveries, among which 6 were total with complete suppression of pain and integral resumption of all the extreme movements of the shoulder. In five cases a painful sensibility to the movements of the shoulder remained. In four cases success was incomplete. The treatment is harmless, the total dose being distributed over three or four weeks. No accidents or incidents were noted; on the contrary, patients benefited by the stimulation exerted by the cortisone on the general condition. The authors noted that their effects were more satisfactory and specially more rapid on the pain than on the block of the shoulder.

Dangers of Nitrous Oxide Anesthesia for Negroes with Sickle Cell Anemia.—Professor Harvier and his associates reported to the National Academy of Medicine the case of a young female Negro native of Martinique who underwent several operations for the correction of dorsal scoliosis. She tolerated anesthesia with sodium pentothal and tubocurarine; and one month later she underwent a second intervention, during which she was given sodium pentothal plus tubocurarine and nitrous oxide. The next day, jaundice of the hemolytic type and acute anemia developed with fever. Scars of leg ulcers were observed, and a hemogram was made, which revealed sickling of the red blood cells. The authors believed that these accidents were provoked by nitrous oxide, the anesthetic that oftenest produces anoxemia. A third intervention performed one year later with the patient under cyclopropane and with superoxygenation was well tolerated.

COMMITTEE ON MENTAL HEALTH

PSYCHIATRIC COMMUNICATIONS PRIVILEGED

At its September meeting the Committee on Mental Health reviewed and discussed the following certified copy of the record of the Circuit Court of Cook County of an opinion filed in the case of Samuel Binder vs. Nathaniel S. Ruvell. This opinion, which was rendered by Judge Harry M. Fisher, was felt by the Committee members to be of such importance to psychiatrists particularly, and to physicians generally with reference to the doctor-patient relationship that it deserved wide publication.

In this case, the patient was receiving psychotherapy under the care of Dr. Roy R. Grinker at Michael Reese Hospital in Chicago. The attorney for the patient's husband requested that the court subpoena Dr. Grinker and the hospital record for testimony in a suit for alienation of affection in which the husband charged the defendant with stealing his wife's (the patient's) affections. The wife had separated from the husband and had instituted suit for divorce.

Both the hospital authorities and Dr. Grinker refused to testify before a notary on the theory that the communications between the patient and the psychiatrist were or should be privileged. A petition was filed before the court seeking an order to command the hospital to produce the records and to command Dr. Grinker to testify. This situation formed the basis for Judge Fisher's opinion.

At the present time there are 30 states that by law recognize the confidential character of conversations between a physician and his patient. Illinois is not one of these states, and, therefore, as no case on precisely this question had ever been presented to the court, the decision rendered here rested upon what the court conceived to be the public policy of the state of Illinois. The Committee believed that similar situations would undoubtedly arise in other states and that this decision might easily be or become a precedent.

RICHARD J. PLUNKETT, M.D., *Secretary.*

Samuel Binder
vs.
Nathaniel S. Ruvell
} Before Harry M. Fisher, J.
No. 52C2535

Tuesday, June 24, 1952

Court met pursuant to adjournment.

PRESENT:

Mr. Samuel J. Andalman,
appeared for plaintiff;

Mr. Frank D. Mayer and
Mr. Francis W. Collopy,
appeared for Michael Reese Hospital
and Dr. Roy R. Grinker.

Mr. Norman Becker,
appeared for Mrs. Eleanor Binder

THE COURT: This suit is one for alienation of affection.

The plaintiff, in pursuit of fact discovery, summoned the Michael Reese Hospital, where Mrs. Binder was a patient recently, to produce the records of her case, and also summoned Dr. Grinker, a psychiatrist in whose charge Mrs. Binder was.

The hospital authorities as well as the doctor appeared before the notary and both refused to testify. A petition was filed here seeking an order commanding the hospital to produce the records and commanding Dr. Grinker to testify. These witnesses justified their refusal on the theory that, this being a psychiatric case, the communications between the patient and the physician are privileged.

It is a case of first impression. No case on the precise question has been presented to the court. And, therefore, the decision here rests upon what the court might perceive to be the public policy of this State.

In this State, so far as I could ascertain, no immunity arises from any professional relationship other than that of lawyer and client and in that case the privilege is one granted to the client, not to the lawyer.

There are, of course, other privileged communications. For instance, communications between husband and wife are privileged. Conversations had in the course of negotiations for settlement or compromise of a claim are privileged. And there are others.

But it is definitely settled that the physician and patient relationship does not enjoy immunity. And I believe it is fair to say that the priest and penitent relationship does not enjoy immunity, although I know of no case and none has been called to my attention where the courts have actually compelled disclosure by the priest of information which came to him in the confessional.

Whether or not communications between a psychiatrist and his patient are privileged, the claim here made by Dr. Grinker goes a little too far. The immunity, if there is one, does not arise out of the mere relationship. The psychiatrist is a physician and the relationship between him and his patient is the same in most respects as the relationship between physician and patient.

The physician can be compelled to testify as to all matters upon which he has an opinion and as to all things he observes as objective symptoms. He may be compelled to testify as to the kind of examination he made. In a proper case he may even be compelled to testify as to the history of the case as it came to him from his patient. He can certainly be compelled to testify as to the diagnosis and prognosis of a case and as to the character of treatment that he advised or applied. In this respect the psychiatrist stands in no better position than the physician does.

However, it is claimed that there is a vital difference in respect of communications between the psychiatrist and his patient and communications between the ordinary physician and his patient. I believe that that is true. The ordinary physician seeks from his patient disclosure of facts relating to a particular malady, insofar as the information might aid him in ascertaining the subjective symptoms; the psychiatrist seeks to ascertain the cause of mental or emotional disturbances of a maladjusted patient. His sphere of inquiry necessarily covers every experience of the patient. He may be interested in knowing the experiences of childhood. That may weigh very heavily with him in determining the cause of the disturbance. He may be interested in the experience of the patient during puberty, during adolescence. In fact, what he seeks to do is to bring back to the conscious memory of the patient things forgotten but which lie dormant in the subconscious mind. He probes deeply, and it is necessary for him to get that information out of the mouth of his patient.

As I recall it, in the early days the men who can be considered as the founders of modern psychiatric treatment, Dr. Freud, Dr. Breuer, resorted to hypnotism in their efforts to penetrate what might be termed the hidden secrets of the patient. That has been largely abandoned and the modern psychiatrist resorts to the slower method of getting the patient to recall forgotten experiences. It doesn't require any scientific knowledge to understand that there can be no success in the effort to ascertain the true cause of the disturbance or in determining the kind of treatment that should be applied unless there is complete confidence in the mind of the patient, not alone in the capacity and skill of the psychiatrist but in the secrecy of the things transpiring in the doctor's chambers. That relationship in that respect is unique and is not at all similar to the relationship between physician and patient.

The question of privilege or privileged communications was examined by Dean Wigmore and he concluded that there are four elements to be considered in determining whether or not immunity exists. He concludes that:

1. The communications must originate in a confidence that they will not be disclosed;

2. This element of confidentiality must be essential to the full and satisfactory maintenance of the relation between the parties;

3. The relation must be one which in the opinion of the community ought to be sedulously fostered; and

4. The injury that would inure to the relation by the disclosure of the communications must be greater than the benefit thereby gained for the correct disposal of litigation.

I think that is a good summary of the factors to be considered by the court in determining the question of whether a communication is privileged or not and particularly the fourth. I think that should be the guiding element, namely, is it, from the social point of view, more important to compel disclosure of a confidential communication so that a particular case be correctly disposed of or is it more important in a particular relationship that the confidences be protected? The question almost answers itself in a case such as this.

Psychiatry is a relatively new science. Its function is to study the operation of the mind and to apply methods of healing where the mind is disturbed. The pursuit of knowledge in that field has been long delayed. And while I am in no position to judge the potentialities of that science as it is now practiced, we do know with a degree of certainty that it has gained world recognition even as early as World War I. In both of the hostile camps, resort to psychiatry was not only frequent but virtually universal. It has been extended to a point where in World War II it was a recognized and respected department of the operations of the military, naval and particularly the air forces. It has even gained recognition in our laws, although it is somewhat doubtful as to whether sufficient progress has been made in that field so that laws can be predicated upon it. Nevertheless, it has gained recognition in our criminal code and in the establishment of psychiatric departments to aid the courts.

Undoubtedly the potentialities of this profession are great. As I have indicated, it may not yet have reached its ultimate strength, but it is progressing. And since it is based on confidence, it is clear that if the courts compel disclosure and thus the abuse of that confidence, that much of the knowledge gained in the study of that science would become abstract and useless as a healing means.

There can be no doubt what the answer should be to the query as to which is more important, the protection of the confidences or the correct disposal of a particular case.

The courts and the law have a high respect for science and are always alert and ready to aid in its progress. They, the courts, seek the help of the scientist in the disposition of their cases, in their quest for truth. The courts allow the scientist to express opinions as evidence where the layman may not do it. And in every respect the courts have shown their high regard for scientific attainment.

Is it conceivable that the courts in a situation such as is presented here today would say, true, you are engaged in the profession of healing the mentally disturbed, the maladjusted members of our society. We know that you cannot do it successfully without probing into the inner recesses of the mind. We know that you cannot do it without obtaining the confidence of your patient and getting the information from him. Nevertheless, it is our job to get all the information we can in order to correctly dispose of a case. Therefore, we are going to compel you to disclose those matters which came to you as a result of your confidential relationship and thereby run the risk of such a disservice to society as may rob it of a healing process affecting thousands and perhaps millions of our inhabitants.

My understanding of the law is otherwise. I am persuaded that the courts will guard the secrets which come to the psychiatrist and will not permit him to disclose them. I am persuaded that it is just one of those cases where the privilege ought to be granted and protected. And the social significance of it is probably even greater than that which comes from the protection of the communications between lawyer and client.

As a matter of fact, the medical profession has moved rather slowly. It is only within our generation that it has made great strides. Out of this very practice of psychiatry may come evidence of values that we have not in the past been able to see. It may even throw light on the value of the confessional, not from a religious point of view but from a psychotherapeutic point of view. It may be that the old adage, "confession is good for the soul" may have greater depth than being a mere adage. There may be therapeutic value in unburdening the things that trouble the mind.

And while generally I am opposed to extending privileges of communications between parties, I think the whole problem needs careful consideration by the courts and, as I have already indicated, in the case of the psychiatrist and his patient, at least that phase of the examination by the physician which requires confidential communications should be protected.

The fact that there is no precedent for it is really of no moment. There cannot be a precedent until the question is presented to the courts for decision. And if evidence of changing conditions or changing knowledge is presented to the court, the court must in some way seek to ascertain what the general community interest demands and what the customs and practices of the people in that respect are and from that pronounce its understanding of the public policy.

Accordingly, I shall hold that all confidential communications between Mrs. Binder and Dr. Grinker are privileged and may not be inquired into. To the same extent, insofar as the records of the hospital may disclose such confidential communications, they are privileged.

Counsel for the plaintiff in his brief suggests that because Mrs. Binder is not a party to this lawsuit, the privilege, if it exists, would not apply. I see no merit in that suggestion at all. The cases cited specifically hold and properly hold that knowledge coming to a lawyer from a client who is not a party to the lawsuit in which the lawyer is asked to testify is not privileged unless it in some way affects the client. Of course, it is true that if it doesn't affect the client, the client has no privilege. But here the patient is Mrs. Binder and it would be she who would be most vitally affected by the disclosures.

That leaves only the question as to whether or not I should direct the hospital to open its records with reference to things which they might show as to the conduct of the patient, which in turn would throw some light upon the issues in the case before me. A simple answer to that would be it would be hearsay. Mrs. Binder is not a party to this lawsuit. Mr. Ruvell is a stranger to those records. It is not a case between the hospital and Mrs. Binder or a case in which Mrs. Binder is a party and it is material to the matters in inquiry as to what happened in the hospital.

Ruvell cannot be bound by what somebody put down on a record in the hospital when there was no relationship between him and the institution. And quite in the same way that would apply, too, as to whether Dr. Grinker should be required to testify as to matters not privileged, and I have indicated what they were, examination, objective symptoms, diagnosis, prognosis, treatment. It has no place in this case.

As a matter of fact, with reference to the records, counsel in his petition specifically says that he wants them mainly for the purpose of impeaching Mrs. Binder and he is showing that there was some conduct, namely, telephone calls, which would throw light upon the matters in issue here. But I have already characterized the nature of Mrs. Binder's testimony. There was nothing there which the records there might or could impeach. But I repeat, whether they do or do not contain evidence which might throw light upon the issues in the case here, that would be hearsay.

Accordingly, the motion to compel the hospital to produce its records and to compel Dr. Grinker to testify will be denied.

The above is a statement by the trial judge of the reasons for his decision and should be included in the report of the proceedings.

Harry M. Fisher,
Judge.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Medical Services: Monopoly in Relation to Prepaid Medical Care Plans.—This was an action by Group Health Cooperative of Puget Sound against the King County Medical Society and others, for money damages and for injunctive relief in connection with the defendants' alleged combination or arrangement in restraint of competition in the field of independent contract medicine and hospital service. From a judgment in favor of the defendants, the plaintiff appealed to the Supreme Court of Washington.

The plaintiff Cooperative is a nonprofit corporation and registered health care service contractor. The defendant Society, a nonprofit corporation, is composed of approximately 950 licensed physicians residing and practicing medicine in King County—all but a very small number of the total of such physicians. The defendant Bureau is an unincorporated association composed of approximately 600 physicians who are members of the Society. The defendant Service Corporation is a nonprofit corporation organized by members of the Society to furnish medical care and hospitalization to the employees of businesses and industries in the county. Defendant Public Hospital District No. 1 of King County (Renton Hospital) is a municipal corporation operating a hospital at Renton, Wash. Defendant Swedish Hospital is a nonprofit corporation operating a hospital in Seattle.

The plaintiffs alleged that the Society, Bureau, and Service Corporation and the members of each, combined, agreed, and conspired: to acquire a monopoly in the furnishing of prepaid medical and hospital care; to eliminate competition and restrain trade therein; to bring about a boycott of any person or organization attempting to furnish such care through physicians not members of the Society; and to injure and hamper physicians and surgeons not members of the Society in the practice of their profession, by the regular practice of intimidation, coercion, threats, libel, and slander. Plaintiffs also alleged that defendants Swedish Hospital and Renton Hospital entered into the combination, agreement, and conspiracy by adopting by-laws or regulations, under which access to the respective hospitals has been denied to any physician not a member of the Society. The defendants denied the allegations respecting an alleged combination, agreement, and conspiracy. They then alleged, by way of affirmative defense, that the plaintiff Cooperative is operating its property as a commercial enterprise and engaging in contract practice in violation of the ethics of the medical profession and in violation of its charter as a charitable corporation.

Contract medicine has been defined in the "Principles of Medical Ethics of the A. M. A., 1949," as follows: "Contract practice as applied to medicine means the practice of medicine under an agreement between a physician or a group of physicians, as principals or agents, and a corporation, organization, political subdivision, or individual, whereby partial or full medical services are provided for a group or class of individuals on the basis of a fee schedule, or for a salary or for a fixed rate per capita." While entertaining the view that almost all of these kinds of agreements involve some evils, the Society has been chiefly concerned with contracts involving private employers, such contracts being known as "industrial contracts."

In 1933, the Society appointed a committee to deal with the problem of industrial contract practice. The report of this committee recommended that, of the several methods that might be pursued, the only practical one was "to organize the members of the profession into a large group to go into competition with the existing organizations contracting for medical, surgical and hospital care, covering the low income group." Pursuant to this suggestion, the Society, in April, 1933, caused the nonprofit Service Corporation and the unincorporated Bureau to be organized. The Bureau is composed of physicians who are under contract with Service Corporation to furnish prepaid contract service to persons covered by industrial contracts negotiated by Service Corporation. The Bureau physicians receive compensation for such services in the form of fees paid to them by the Service Corporation. Both the Bureau and Service Corporation have at all times been composed exclusively of Society members, all members of the Society being urged to join. There is close coordination between the three organizations, including joint meetings. Membership in the Bureau is denied to physicians who engage in any competing industrial contract practice, and Bureau members who turn to such practice are dropped from membership. The availability of prepaid service offered by Service Corporation is confined to persons as determined from time to time by the Society, Bureau, and Service Corporation. At the present time, Service Corporation administers some 2,500 industrial contracts in King County, involving approximately 80,000 subscribers for medical care. The income under these contracts aggregates about $375,000 a month. The net income, after payment of expenses incurred by the corporation, is distributed to Bureau physicians in the form of fees. In the view of Society officials, this industrial contract plan eliminates the objectionable features of contract practice as it existed prior to 1933.

While the Society has long exerted its influence in opposition to industrial contract practice, it did not originally deny membership to physicians, otherwise qualified, who engaged therein. Consequently, when the Society established its competing industrial contract plan in 1933, there were from 50 to 75 members then engaged in such practice under other plans. From that time forward, however, the Society adopted a careful screening process for the purpose of denying membership to all new applicants engaged in such practice. Furthermore, in order to force discontinuance of such practice by those already enjoying Society membership, or by those who thereafter sought to join the Society, the by-laws of the Society relating to disciplining of members was amended by adding a clause providing that members . . . "who shall engage in contract practice unless the same shall previously have been authorized by the Board of Trustees of this Society, or who as physicians or surgeons shall serve on the staff of or perform work for the patients of, or shall perform work in, any institution or group or organization unless such services or work shall previously have been authorized by the Board of Trustees of this Society, shall be liable to censure, suspension or expulsion." This by-law amendment, together with the new screening process on application for membership, proved very effective in curbing industrial contract practice other than that sponsored by Service Corporation. Most members who were then engaged in "unauthorized" contract practice discontinued such practice; however, two residents of Tacoma, Dr. A. W. Bridge, operating his Bridge Clinic, and L. G. Prendergast, operating his State Clinic, later named Medical Security Clinic, Inc., continued to carry on industrial contract medicine in King County in competition with the Service Corporation.

In 1946 the plaintiff Cooperative was organized by leaders in granges, labor unions, and consumer cooperatives in the area. Each member of the Cooperative, by paying the required monthly dues, is eligible to receive prepaid medical and hospital service for himself, members of his family, and dependents. The Cooperative also renders services under industrial contracts, and it is with respect to these industrial contracts that friction has developed between defendants and plaintiffs. The Society and its affiliates are apparently willing to tolerate the Cooperative's prepaid service to its own members, providing it will discontinue the industrial contracts. It is not feasible, from an economic standpoint, however, for the Cooperative to discontinue its industrial contract practice, even if the Cooperative were otherwise willing to do so. The Cooperative employs three salesmen who devote their time largely to selling industrial contracts. The Cooperative does no advertising but issues a brochure that explains the plan and emphasizes the reasons why employees should subscribe to it. The Cooperative has in its employ 20 licensed physicians, and the relationship between the Cooperative and its professional staff is regulated by the organization's by-laws and by a contract between the two, the by-laws providing that "Neither the Board of Trustees nor the membership shall supervise, regulate or intervene in the professional relationships between the physicians and

their patients." The testimony is undisputed that this provision has been observed at all times "to the letter." All physicians retained by the Cooperative are satisfied with their employment, and there has been no dispute of any kind with them. In the fall of 1946, the Cooperative bought the capital stock of Medical Security Clinic, Inc. The Cooperative's purpose in purchasing Medical Security Clinic was apparently twofold: to acquire needed hospital facilities, and to obtain a large block of industrial contracts. It was recognized that the Cooperative's income from its member-patients was insufficient and that future success depended on developing an industrial contract practice. The staff of Medical Security Clinic was retained, but this does not mean, however, that the Prendergast policies, so bitterly criticized by the Society, were continued in effect after the Cooperative acquired the capital stock of Medical Security Clinic, Inc. After the purchase, the Cooperative's policies, as set forth in its by-laws and in the staff contract, governed. All medical service was thereafter rendered in the name of the Cooperative. While the name "Medical Security Clinic Division" also appears in the heading of industrial contracts thereafter negotiated, this is apparently only for the purpose of establishing the Cooperative as the clinic's successor in interest. Medical Security Clinic, as a corporation, has been inactive since the purchase. It performs no business whatsoever, except to elect officers and file federal income tax returns. It has no employees, maintains no bank account, and renders no medical service.

In 1948, the A. M. A. officially entered Group Health Hospital on its hospital register. Before doing so, an investigation was made by the Council on Medical Education and Hospitals of the A. M. A. A report covering this investigation, which called specific attention to the method of contract practice employed by the Cooperative, was followed by affirmative action registering the hospital. It may be fairly inferred from this that the hospital plant, facilities, and staff were found to be in compliance with A. M. A. standards. We conclude, said the Supreme Court, that plaintiff physicians, Medical Security Clinic, and Group Health Hospital are not now rendering professional service of a quality substantially below that rendered by the average physician, surgeon, clinic, or hospital in the community.

The Society's antagonism to all "unauthorized" contract medicine plans, including the Cooperative's plan, is predicated primarily on the premise that they preclude "free choice of physicians." The Cooperative's plan permits persons to determine whether they wish to become beneficiaries under the plan; permits beneficiaries free choice of all physicians and surgeons participating in the plan; permits such beneficiaries (at their own expense) to go to other physicians and surgeons for treatment of any particular ailment without terminating the plan; and permits such beneficiaries to terminate their participation in the plan by simply declining to pay the next month's dues. The Cooperative plan does not permit beneficiaries to receive, as part of their benefits under the contract, the services of nonparticipating physicians. It is to be noted, however, that the Service Corporation plan also restricts beneficiaries thereunder to a choice limjted to participating physicians. While such beneficiaries have a choice of 650 physicians who have joined the Bureau, they are denied the right to choose any of the 350 or so members of the Society who have not elected to join the Bureau, or any of the 20 Cooperative physicians who are, as long as they continue their present practice, denied the right to join the Bureau. Thus the Cooperative's industrial contract plan appears to accord "free choice of physician" quite as much as does the Service Corporation plan. In addition to the question of "free choice of physicians" there were other A. M. A. ethical standards that had to be considered. One of these matters pertained to the question of "solicitation." The evidence in relation to this point consisted of the testimony of Don A. Northrop, general manager of Group Health Clinic and Group Health Hospital, that his organization is soliciting new subscribers and new industrial accounts. There is nothing in the record to indicate that there is any misrepresentation, overselling, or other impropriety with respect to the way in which this soliciting is done. There would seem to be no more objection to such solicitation, from the standpoint of professional ethics or general public interest, than in the case of Service Corporation's solicitation. The latter organization engages a force of paid salesmen and does extensive newspaper and radio advertising in the sale of its industrial contracts. We find, said the court, that the evidence bearing on the objections set out above fails to establish any grievance against the Cooperative based on ethical considerations.

As previously indicated, the Cooperative provides service under two kinds of contracts—its membership contracts and its industrial contracts. Both kinds would seem to fall under the ban of the Society's by-laws, yet the Society has made it clear time and again that plaintiff physicians and their associates will be accepted into the Society if they discontinue the industrial practice, even though they continue practice under their membership contracts. It has already been noted that competition between the Service Corporation on the one hand and the Cooperative on the other pertains only to industrial contracts. This fact alone is sufficient to indicate that the Society's primary motive in opposing the Cooperative and its staff members is to restrain the competition that the Cooperative provides through its industrial contracts. The Society's attitude in tolerating contract practice by members who serve fraternal organizations and petroleum companies is also indicative of the Society's underlying purposes referred to above. Relative to the matter of competition between prepaid medical plans, the evidence further indicates that it is the policy of the A. M. A. that "the people should be free to purchase the type of health security they desire."

The plaintiffs alleged that the defendants committed overt acts of various kinds that proved directly injurious to the plaintiffs and that entitled them to monetary damages and injunctive relief. After discussing the evidence relating to these acts and after finding that some acts were performed and some were not, the Supreme Court pointed out that this alone, however, was not sufficient to justify reversal. The plaintiffs were not entitled to prevail unless all of the facts, as here found, gave rise to a cause of action in their behalf.

We will first consider, said the court, whether plaintiffs established a cause of action against the Society and its named officers, the Bureau and its members, and the Service Corporation. The plaintiffs advanced several theories in support of their position. The one first presented and primarily relied on is that the defendants have been engaged in an unlawful combination or conspiracy in restraint of competition and for the purpose of establishing a monopoly.

The Supreme Court said that three elements must be present in any relationship in order to constitute a monopoly or trust within the meaning of the State Constitution. There must be a contract, combination, or other arrangement between two or more corporations, copartnerships, or associations; it must relate to some product or commodity; and its purpose must be to fix prices, limit production, or regulate the transportation of such product or commodity. The court determined that the first two elements were present and then went on to discuss whether or not the combination or other arrangement relative to defendant's medical and related services has for its purpose the fixing of prices or the limiting of production of such products. All members of the Bureau, said the court, bound themselves to render service under the contracts sold and administered by Service Corporation. The terms of such contracts, including the services available thereunder and the prescribed monthly payments, were dictated by Service Corporation, acting for the combination. All members of the Bureau and Society bound themselves to render no other contract service. They then pursued a course of conduct designed to prevent others from rendering any competing contract service. Thus the purpose of the combination was to limit production and, incidentally, to fix the prices to be charged for contract medicine service. There is a well-settled rule, however, that the provisions of the State Constitution do not condemn price fixing and the limitation of production per se but only when either of these results are brought about in connection with a monopoly, with resulting unreasonable restraint on competition. It is necessary to determine whether defendants' combination or arrangement by which production is limited and prices are fixed with respect to prepaid medical service amounts to a "monopoly" in the constitutional sense. There can be no question but that the purpose of the combination in the instant case is to preempt and control all contract medicine practice in King

County. If defendants are successful in this effort, there will be no competition in the contract medicine field. Members of the public will have no opportunity to choose between two or more plans offering this type of service. The result will be a complete monopoly of this product throughout the county. The defendants contend that there can be no monopoly because all qualified physicians are entitled to join the Society and participate in Service Corporation's medical plan. Applicants for membership in the Society, however, are required to discontinue their industrial contract practice, and Service Corporation, a member of the combination, is itself engaged in providing that kind of service. Thus the public would be deprived of all competition in the contract medicine field and could, as pointed out above, be completely denied such service. Defendants also resist being characterized as a monopoly on the ground that the prime purpose of the Society and its affiliates is to uphold the quality of professional service being rendered in King County and to maintain proper ethical standards in the profession. The great public service that medical associations render in developing and maintaining high standards of professional conduct and practice is a matter of general knowledge. The record amply demonstrates that in numerous respects, and over a great many years, the Society has rendered valuable service in this direction. We do not intend to imply by anything said in this opinion that the Society may not adopt reasonable and effective methods of preserving the high quality of service and the high ethical standards of the profession. The facts, however, do not bear out the contention that the defendants' course of conduct is necessary because of the quality of professional service rendered by plaintiffs or because plaintiffs are practicing medicine in an unethical manner. We have found that the quality of professional service rendered by plaintiffs is not substantially below the quality of service rendered by the average physician, surgeon, clinic, or hospital in the community. We have also found that plaintiffs' manner of practice is not "unethical" in the sense used by the A. M. A., or as the term is generally understood by laymen. It may also be noted that the contract practice of medicine, as carried on by plaintiffs, does not constitute "unprofessional conduct" as that term is defined in the state laws. The Society, in characterizing plaintiffs' contract practice as "unethical," is making an unusual and arbitrary application of that opprobrius term. It uses the term to castigate those who seek only to carry on contract practice independent of and in competition with Service Corporation. In our opinion, the Society may not, through the mere use of the term "unethical," clothe with immunity acts that would otherwise fall under the ban of the antimonopoly provision of our Constitution. It is our conclusion, on this branch of the case, that the limitations on production and the price fixing shown to exist here are being consummated in connection with a monopoly as that term is defined in the State Constitution. It therefore appears that, in the relationship established and course of conduct pursued by defendants, there are present all three elements essential to the establishment of a monopoly or trust, within the meaning of the Constitution. There is a combination or other arrangement between two or more corporations and associations; it is concerned with the production and sale of a product—prepaid medical and hospital service; and the purpose of the combination is to limit the production and fix the prices of that service with the object in view of restraining competition and creating a monopoly. The defendants are therefore acting in violation of the antimonopoly provision of the Constitution.

Finally, said the court, we come to a consideration of the affirmative relief to which the plaintiffs are entitled as against the Society, Bureau, Service Corporation, their named officers, and the members of the Bureau. Several kinds of overt acts were alleged and proved in connection with the combination or arrangement in restraint of competition here found to exist. The two kinds of overt acts that are most effective and damaging in this connection are those relating to the exclusion of plaintiff physicians from membership in the Society and those that tend to prevent or discourage members of the Society from consulting with plaintiff physicians or rendering professional services in association with such physicians or for their contract patients or at Group Health Hospital. It is our conclusion that the Society, its officers, and board of directors should be enjoined from following any course of conduct, whether through observance of the provisions of the Society's by-laws or otherwise, that will have the effect of excluding applicants from membership in the Society on the sole ground that they are practicing contract medicine in substantially the manner followed by plaintiffs, or that will have the effect of preventing or discouraging members of these organizations from consulting with plaintiff physicians or rendering professional services in association with plaintiff physicians, or for the latters' patients at any hospital on the sole ground that such physicians or such hospitals are practicing, or providing facilities for the practice of, contract medicine in substantially the manner followed by the plaintiffs. Another class of overt acts that has been particularly effective and damaging in connection with the restraints that defendants here sought to impose, relates to the defendants' efforts to obtain the exclusion of plaintiffs from hospital medical staffs. It is therefore our conclusion that the Society, Bureau, Service Corporation, their board of trustees, officers, and members should be enjoined from following any course of conduct of the kind described above or otherwise, which has for its purpose the exclusion of plaintiff physicians from the hospitals of King County on the sole ground that they are practicing contract medicine in substantially the manner followed by the plaintiffs. It is further held to be to the interests of the parties that the court shall retain jurisdiction of this case for a period of three years from the date of entry of the decree.

With the exception of the judgment as to Swedish Hospital, which was affirmed, the judgment in favor of the defendants was therefore reversed and the cause remanded with instructions to enter a decree conforming to the views expressed in this opinion. *Group Health Cooperative of Puget Sound et al. v. Kings County Medical Society et al., 237 P. (2d) 737 (Washington 1951).*

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

CORRECTIONS IN INTERNSHIPS AND RESIDENCIES

The following approved programs were incorrectly listed in the Internship and Residency Number (*J. A. M. A.*, vol. 150, no. 4 [Sept. 27] 1952). It is suggested that these corrections be made in the lists of approved programs previously published in the Internship and Residency Number. The corrected data for these hospitals are as follows:

Los Angeles County Hospital, Los Angeles, Calif.

The program in pathology, as listed on page 332, should have indicated approval for three years in both pathologic anatomy and clinical pathology.

St. Joseph's Hospital, Denver, Colo.

The chiefs of services of the departments indicated below should have been listed as follows:

Internal Medicine (page 309)
Chief of Service—William Hay

Obstetrics and Gynecology (page 318)
Chief of Service—Lyman W. Mason

Surgery (page 354)
Chief of Service—J. M. Foster

Delaware State Hospital, Farnhurst, Del.

The program in psychiatry, as listed on page 342, should have indicated approval for three years.

Mount Sinai Hospital, Miami Beach, Fla.

The internship program, as listed on page 284, should have indicated additional approval for residency training in the specialties.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Indust. Hyg. & Occup. Med., Chicago

6:93-198 (Aug.) 1952

Relation of Particle Size of Uranium Dioxide Dust to Toxicity Following Inhalation by Animals. II. H. B. Wilson, G. E. Sylvester, S. Laskin and others.—p. 93.
Observations of Cardiorespiratory Performance in Normal Subjects Under Unusual Stress During Exercise. R. A. Bruce, F. W. Lovejoy, P. N. G. Yu and M. E. McDowell.—p. 105.
Castor Bean Pomace Exposure. M. A. Snell.—p. 113.
Fatal Exposure to Methylene Chloride Vapor. S. Moskowitz and H. Shapiro.—p. 116.
Instruments for Measuring Secondary Radiation. W. W. Van Allen. —p. 124.
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Anticholinesterase Activity of Tributyl Phosphate. J. C. Sabine and F. N. Hayes.—p. 174.

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Outpatient Treatment of Congestive Heart Failure with Sodium-Removing Exchange Resins. R. S. Aaron and R. E. Weston.—p. 182.
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Virus Influenza A' Infection with Pulmonary Manifestations. J. M. Scher and E. Jaruszewski.—p. 201.
Mumps Arthritis. E. Appelbaum, J. Kohn, R. E. Steinman and M. A. Shearn.—p. 217.
Clinical Study of Gitalin. M. R. Hejtmancik and G. R. Herrmann. —p. 224.
Tendency Toward Hypotension in Left Lateral Recumbency. P. Stein. —p. 234.

The Liver in Obesity.—After careful screening to exclude all past or present illness that might affect the liver, 20 men who were between 50 and 100% overweight were studied for liver disturbance by laboratory tests and needle biopsy. The men, who were from 23 to 71 years old, all had both laboratory and microscopic evidence of liver disease. Approximately half of the obese patients showed impairment of dextrose tolerance, but none required insulin. The carbohydrate tolerance failed to correlate with other evidences of liver disease. The sulfobromophthalein (bromsulphalein®) retention was abnormal in all 20 patients. Thymol turbidity and the serum cholesterol level were abnormal in 10. One-third showed abnormally high urobilinogen outputs in the urine. One-fourth had high serum alkaline phosphatase levels. Cephalin-cholesterol flocculation and cholesterol ester ratios were abnormal in one-fifth of the group. Serum albumin and globulin were normal in all persons tested. Degenerative changes of the parenchymal cells, fatty change, bile pigment retention, parenchymal cell regeneration, and periportal fibrosis were present to at least a moderate degree in approximately half of the men. One-third of them showed more than slight cellular infiltration of the periportal spaces. In none was the liver entirely normal. The duration of the obesity, ranging from 8 to 60 years, but not its degree, proved significantly related to the extent of anatomical disturbance of the liver. The liver function tests did not show comparable correlation. The liver damage in obesity may be explained by (*a*) the high caloric requirement of obese persons, constituting a functional overload on the liver; (*b*) the high-carbohydrate, high fat, low protein diet customary among the obese; and (*c*) the increased requirement of choline and vitamins of the B complex imposed by the quantitative and qualitative nature of the obesity diet. The reducing program should consist of a high protein diet supplemented by choline and vitamins of the B complex.

Primary Pulmonary Arteriolosclerosis.—The occurrence of primary pulmonary arteriolosclerosis is reported in two women, aged 26 and 29, and in one man, aged 64. The authors define primary pulmonary arteriolosclerosis as a rare, progressive, fatal disease of unknown causation characterized by extensive narrowing of the pulmonary arterioles due to an arteriosclerotic process. Initially the symptoms are predominantly those of respiratory insufficiency, such as dyspnea, cough, hemoptysis, and cyanosis. In this phase, pulmonary hypertension has developed and there is pulmonary arteriosclerosis, but there is not yet an overwhelming work load on the cardiac musculature. As the disease progresses, cardiac decompensation ensues, and its signs and symptoms are then superimposed on the preexisting clinical picture. The resultant picture is best described clinically as that of right heart failure with venous distention, progressive peripheral edema, passive congestion, and development of effusions in the pleural, peritoneal, and pericardial cavities. The absence of pulmonary congestion in the presence of obvious cardiac failure is striking. Necropsy was performed in two of the authors' patients, and a biopsy specimen of the lingula was obtained by exploratory thoracotomy in the third patient. Microscopic observations showed that the outstanding pathological lesion is a severe fibrous intimal thickening of the pulmonary arterioles, as well as hypertrophy and dilatation of the right ventricle. The diagnosis may be suspected during life by detailed clinical evaluation, but is established with reasonable certainty only by microscopic examination of a lung biopsy specimen. Special reference is made to similar lesions of the pulmonary arterioles occurring during the course of diseases of the heart, of diseases producing diminution of functional lung volume, and of vascular diseases of the lungs. As in other diseases of unknown causation, numerous etiological theories have been offered for primary pulmonary arteriolosclerosis. The role of primary or essential pulmonary arterial hypertension with resultant vascular hypoxia is discussed.

A.M.A. Arch. Ophthalmology, Chicago

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*Toxoplasma Chorioretinitis in Adults. H. C. Wilder.—p. 127.
Cerebral Electric Response to Intermittent Photic Stimulation in Amblyopia ex Anopsia: H. M. Burian and C. W. Watson.—p. 137.
Comparison of Results of Cortisone Treatment by Instillation and by Sub-Conjunctival Injection: Experimental Study. I. C. Michaelson. —p. 144.
Clinical Evaluation of Aqueous-Flow Test: Preliminary Report. A. de-Roetth Jr. and W. S. Knighton.—p. 148.
Congenital Ectasia of Cornea. H. C. Donahue.—p. 154.
Pharmacology and Toxicology. I. H. Leopold.—p. 163.

Toxoplasma Chorioretinitis in Adults.—Organisms morphologically indistinguishable from Toxoplasma organisms were found in chorioretinal lesions in 53 eyes in the registry of ophthalmic pathology. Specimens were sent in from all sections of the United States. The patients were from 14 to 83 years of age at the time of enucleation, and eye symptoms had been observed for from a few weeks to 32 years. Thirteen patients gave a history of direct injury to the eye but in only three was the eye penetrated. The eyes were usually blind and painful at the time

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Titles marked with an asterisk (*) are abstracted.

of enucleation, although pain tended to be intermittent. In 37 cases the clinical diagnosis was uveitis, and in 9 of these the uveitis had been regarded as tuberculous. Serum was obtained from only three patients. Dye tests, as recommended by Sabin and Feldman, were performed in three cases. A dye test titer of 1:64 was obtained on two patients. In another, whose eye had been enucleated six years earlier, the dye test titer was 1:256. The lesions in which the organisms were found were all strikingly alike and focally involved the retina, the choroid, and frequently the sclera. The organisms were found in the necrotic portion of the retina in the focal granulomatous chorioretinal lesions. Crescentic forms were often arranged in pairs or rosettes, whereas spherical forms commonly occupied pseudocysts. In the registry of ophthalmic pathology, among 131 eyes with the pathological diagnosis of tuberculosis or possible tuberculosis, identical protozoa have been demonstrated in 30, whereas in only 3 have tubercle bacilli been found, although all the suspected lesions have been subjected to acid-fast staining and careful search.

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Topical Anesthesia in Bronchoscopy. H. J. Rubin and B. M. Kully. —p. 13.

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Neoplasm of Nasopharynx: Review of 68 Cases Which Appeared in the Japanese Literature. T. Daito, H. Sakamoto and H. J. Hara.—p. 45.

Cholesteatoma in Radical Mastoidectomy Cavity Secondary to Use of Primary Skin Grafts. N. V. Peterson.—p. 49.

Functional Examination of Hearing. A. Lewy, S. L. Shapiro and N. Leshin.—p. 61.

American Journal of Clinical Pathology, Baltimore

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Fatal Poisoning Due to Cationic Detergent of Quaternary Ammonium Compound Type. L. Adelson and I. Sunshine.—p. 656.

Cytologic Observation on Effect of Progesterone on Cervical Tissue in Squamous-Cell Carcinoma of Cervix. L. I. Platt.—p. 662.

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Prevalence of Carriers of Leptospira and Salmonella in Norway Rats of Baltimore. Huan-Ying Li and D. E. Davis.—p. 90.

American Journal of Psychiatry, New York

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Peptic Ulcer: Incidence and Diagnosis in Psychotic Patients. B. M. West and A. O. Hecker.—p. 35.

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Lumbar Sympathectomy in Peripheral Vascular Diseases. K. C. Olson and B. L. Leming.—p. 202.

Diseases of Urachus, with Three Illustrative Case Reports. E. P. Carreau and G. A. Higgins.—p. 205.

Postmortem Cesarean Section: Surgical and Legal Aspects. H. P. Lattuada.—p. 212.

*Chronic Appendicitis or Painful Ovary? G. D. Patton.—p. 215.

Partial Gastrectomy for Duodenal Ulcer.—Partial gastrectomy was done on 99 patients with duodenal ulcer. The ulcer was removed in all cases. Gastrojejunal anastomosis was of an antecolic type, using a short afferent jejunal loop. The postoperative mortality rate was 3.03%. The over-all results are considered excellent to good in 87% of the cases that were followed up. There were two cases of marginal or stomal ulcer. Atelectasis was the most frequent postoperative complication and occurred in eight patients. There were no cases of wound disruption or postoperative hernia in this series of cases in which a supraumbilical, transverse, elliptic incision was used. The end results of this antecolic anastomosis are comparable to those reported in series in which a retrocolic anastomosis was performed.

Chronic Appendicitis or Painful Ovary?—Because patients who consult gynecologists for pain in the right lower quadrant of the abdomen frequently give a history of previous appendectomy for chronic appendicitis, Patton decided to study this problem in two groups of 100 patients who had undergone appendectomy for chronic appendicitis. It was found that 78% of cases of chronic appendicitis occur in women and more than three-fourths of women with chronic appendicitis are between the ages of 11 and 25, the same years that the ovaries are establishing their cyclical activity. Of the women who had appendectomies for "chronic appendicitis," 79.5% returned with signs and symptoms of ovarian dysfunction; 74.2% of these had pain in the right lower quadrant of the abdomen. It is suggested that right lower quadrant pain attributed to chronic appendicitis in women is frequently due to a painful, tender ovary.

Am. Practitioner & Digest of Treatment, Philadelphia

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What to Tell Patient with Simple Glaucoma. R. I. Pritikin and M. L. Duchon.—p. 531.
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Role of Sympathetic Block in Treatment of Chronic Phlebitis and Post-Phlebitic Syndrome. J. E. Ruben.—p. 569.

3:605-692 (Aug.) 1952

*Combined Caffeine and Ergotamine in Heat Exhaustion. J. A. M. Meerloo.—p. 605.
Precocious Metastases. W. C. Matousek.—p. 608.
Chronic Porphyria: Report of Two Cases, One of Which was Treated with ACTH and Cortisone. J. B. Meyers and R. L. Griffith.—p. 612.
Unusual Congenital Cardiac Anomaly with Associated Anomalous Venous Return: Sudden Death. F. B. Schultz.—p. 616.
Some Clinical Aspects of Potassium Metabolism. W. W. Engstrom. —p. 623.
Tests of Adrenal Cortical Function. W. W. Engstrom.—p. 626.
Surgery of Adrenal Tumors. F. Hinman Jr.—p. 631.
Lanatoside C in Treatment of Supraventricular Tachycardia. R. M. Levenson and R. H. Thayer.—p. 635.
Treatment of Constipation in Pregnant Women. M. C. C. Lilienfeld. —p. 638.
Current Therapy of Dysenteric and Diarrheal Amebiasis. W. A. Sodeman. —p. 640.
Premalignant Lesions and Early Diagnosis of Breast Carcinoma. H Wammock.—p. 642.
Treatment of Skin Diseases with Adrenocorticotropic Hormone and Cortisone. C. J. Dillaha and S. Rothman.—p. 646.
More Recent Aspects of Chronic Pulmonary Disease. E. Mayer.—p. 650.

Combined Caffeine and Ergotamine in Heat Exhaustion.—During the war Meerloo frequently saw heat exhaustion associated with anxiety and nervousness, and a combination of ergotamine and caffeine was found helpful in these cases. The immediate symptomatic effect was so gratifying that the patients spoke of "wonder pills." The preparation used contains 1 mg. of ergotamine tartrate and 100 mg. of caffeine. Caffeine is effective in heat exhaustion and has been used as a stimulant. It is a powerful central nervous system stimulant. Ergotamine tartrate acts on the involuntary smooth muscles. It constricts the small blood vessels, thus producing an increase in the blood pressure. The author briefly describes cases in which he has used this treatment since the war. He found that the drugs were well tolerated if given in doses of 1 or 2 tablets, but he warns that it should not be prescribed in cases of peripheral vascular diseases or in pregnancy. The usual palliative measures, such as rest, fluid intake and additional salt intake, should be used in addition to the medication.

Blood, New York

7:765-862 (Aug.) 1952

Erythremic Myelosis (Di Guglielmo's Disease): Critical Review with Report of Four Cases, and Comments on Erythroleukemia. S. O. Schwartz and J. Critchlow.—p. 765.
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Non-Wettable Surfaces. J. L. Tullis and E. G. Rochow.—p. 850.

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Effect of Irradiation Upon Uptake of Labeled Phosphorus in Human Carcinoma of Cervix. M. L. Taymor, N. Gold, S. H. Sturgis and others. —p. 469.
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Plasma-Cell Tumors of Mouth and Upper Air Passages. M. R. Ewing and F. W. Foote Jr.—p. 499.
Case of Acute Plasma-Cell Leukemia Supporting Concept of Unity of Plasmacellular Neoplasia. W. Newman, W. C. L. Diefenbach, M. Quinn and L. M. Meyer.—p. 514.
Carcinoma Arising in Bronchiectatic Cavities. B. E. Konwaler and I. M. Reingold.—p. 525.
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*Subnormal Response to Cream in Cancer Patients. J. M. Waldron, B. Beidelman and G. G. Duncan.—p. 583.
Effect of Multiple Visceral Excisions on General Nutritional Status: Experimental Study in Relation to Radical Surgery. G. F. Robbins and A. Brunschwig.—p. 589.

Trichomonas Infestation and False Diagnosis of Squamous Cell Carcinoma.—The lesion of the cervix uteri variously termed "carcinoma in situ," "intraepithelial carcinoma," and "preinvasive carcinoma" has been widely accepted as a diagnostic entity. Disagreement has arisen, however, as to the criteria needed to make such a diagnosis from tissue. When the authors first used the Papanicolaou cell smear test, they had a relatively large number of false positive smears. Review of these smears revealed that atypical changes resulting from Trichomonas infestations was responsible for most of the errors. Since they began taking Trichomonas infestations into account, the incidence of false positive diagnoses has dropped to less than 1% of all positive smears. As the result of overcautiousness, however, false negative reports have been made in cases of true cancer complicated by trichomonad infestations. It was also discovered that the presence of this organism and its associated cell atypia, superimposed on radiation changes in a smear from a patient who has been treated for carcinoma, can produce a most difficult diagnostic problem. The authors compare the atypical cervical epithelial changes appearing in both smears and biopsies as a result of Trichomonas infestations with the changes that they regard as consistent with the diagnosis of carcinoma in situ. They discuss observations on 26 cases that illustrate the various cytological and histological features of both reversible and irreversible changes. They found that carcinoma in situ tends to be anaplastic. The lesion starts in the germinal layer of the epithelium and progresses outward in an irreversible process. Atypical changes caused by trichomonad infestation start in the outer portions of the epithelial layer and progress inward. They are reversible. The authors found that much greater attention must be paid to obtaining endocervical samples with the sharp curette and that multiple sections must be made of the biopsy material. Cytological samples must also be obtained repeatedly; only the comparison of repeated samples with initial samples can answer the question of reversibility. Faith in the ordinary cervical biopsy taken at the squamocolumnar junction has been somewhat shaken. In many cases of early carcinoma of the cervix the endocervical material alone contained the tumor.

Subnormal Response to Cream in Cancer Patients.—Previous studies had shown that the ingestion of various fats such as olive oil, corn oil, cottonseed oil, and cream from cow's milk reduces the coagulation time of the blood of humans and dogs. Because of the frequent use of cream in the treatment of gastro-

intestinal bleeding, the effect that cream had on blood coagulation was investigated more extensively. Studies on 100 patients disclosed that in the small group that did not show an appreciable decrease in coagulation time after drinking cream cancer was the only common feature. Since then an additional group of 130 patients have been studied. All patients fasted for 8 to 10 hours before the study, which consisted of obtaining a control fasting coagulation time and then administering 60 cc. of cream. The coagulation time was then determined one-half hour, one hour, two hours, and three hours after the ingestion of the cream. Control experiments were done in which the patients were fed water in place of the cream. Of the total 230 patients, 55 had cancer and 175 had other diseases. The cancer patients showed a subnormal response to the in-vivo clot accelerating properties of cream. The occurrence of this subnormal response is independent of the type or site of cancer. It is also independent of certain factors common to cancer patients, such as elevated sedimentation rate, level of plasma protein, and state of nutrition.

Cancer Research, Chicago

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Observations on Carcinogenesis by 4-Dimethylaminoazobenzene. P. N. Harris and G. H. A. Clowes.—p. 471.
Estimation of Nucleic Acids in Individual Isolated Nuclei of Ascites Tumors by Ultraviolet Microspectrophotometry and Its Comparison with Chemical Analysis. C. Leuchtenberger, G. Klein and E. Klein.—p. 480.
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Circulation, New York

6:1-160 (July) 1952

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Sympathectomy for Essential Hypertension. E. V. Allen.—p. 131.

Delaware State Medical Journal, Wilmington

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Surgery and Antibiotics. E. G. Laird.—p. 165.
Use of Antibiotics in Neurosurgery. P. D. Gordy.—p. 167.
Antibiotics in Orthopedic Surgery. W. L. Bailey.—p. 168.
Antibiotics in Gynecology. S. W. Rennie.—p. 169.
Antibiotics in Urology. J. H. Furlong Jr.—p. 170.
Chemotherapy in Ophthalmology and Otolaryngology. W. T. Reardon.—p. 172.
Antibiotics in Cardiovascular Diseases. J. R. Durham.—p. 173.
Antibiotics in Treatment of Pulmonary Diseases and Meningitis. G. B. Heckler.—p. 174.
Antibiotics and Their Use in Diseases of Gastrointestinal Tract. I. L. Chipman Jr.—p. 176.
Antibiotic Sensitivity Testing. E. G. Scott.—p. 178.

Georgia Medical Association Journal, Atlanta

41:277-332 (July) 1952

Primary Carcinoma of Liver: Review and Case Report in Colored Juvenile. C. C. Lamb and F. F. Wood.—p. 279.
Hematuria. R. Bell and R. F. Stinson.—p. 281.
Care of Female in Climacteric. R. A. Ross.—p. 283.
One Hundred Consecutive Partial Gastrectomies for Benign Peptic Ulcer. J. W. Turner and A. B. Turner.—p. 287.
Review of 200 Cases: Early Diagnosis and Treatment of Congenital Dislocation of Hip. J. H. Kite and R. E. King.—p. 291.
Surgical Treatment of Residual Fibrocaseous Nodules in Pulmonary Tuberculosis. R. F. Corpe, W. H. Kasserman and H. T. Randsell.—p. 295.
*Adrenocortical Insufficiency Observed in Three Male Infants in One Family. M. H. Roberts and P. F. Baehren.—p. 299.
Recent Advances in Physical Therapy Applied to General Practice. A. M. Pruce.—p. 305.

Adrenocortical Insufficiency.—Three brothers in the neonatal period and infancy had a striking symptom complex consisting of persistent, projectile vomiting, recurrent and intractable dehydration, and occasional periods of cyanosis and shock. Although adrenocortical insufficiency was suspected in all three infants, the presence of congenital adrenocortical hyperplasia was proved conclusively in only one by necropsy. Adequate laboratory data were not available to establish the diagnosis before death. Hemoconcentration, low blood sugar level, and elevated nonprotein nitrogen level were suggestive findings. Gastrointestinal roentgenograms indicated partial obstruction at the pylorus in two of the infants, with normal pattern in one. Vomiting became so severe in one patient that a laparotomy was done, but no abnormalities were revealed. None of the infants showed any evidence of increased pigmentation; no macrogenitosomia was evident. One infant died at the age of 7 months and 5 days, one at 4 months and 12 days, and one when only 34 days of age. The patient with the longest duration of life showed striking improvement when adrenocortical extract and sodium chloride were administered. It seems likely that had adrenocortical extract been increased to adequate amounts or desoxycorticosterone been substituted, the infant might have survived a longer period. The family history of the patients was entirely negative. There was a normal sister who was the product of the mother's second pregnancy. A review of the case reports of adrenocortical insufficiency in infancy collected from the literature indicates that in the male macrogenitosomia almost invariably occurs, although its appearance may be delayed as late as four years of age. The authors' three patients who died in the early months of life did not show any abnormality of genitalia or virilism.

Iowa State Medical Society Journal, Des Moines

42:287-388 (July) 1952

Current Trends in Antibiotic Therapy. W. E. Herrell.—p. 287.
*Psychotic Reactions Associated with ACTH and Cortisone. G. Tourney and J. S. Gottlieb.—p. 292.
Anesthesia in the Aged. H. M. Livingstone and N. P. Johnson.—p. 296.
Central Serous Choroidosis. G. L. Walker.—p. 303.
Tendon Transfers in Forearm and Hand. W. C. Graham.—p. 305.

Psychotic Reactions Associated with Corticotropin and Cortisone Therapy.—Mild mood disturbances in the form of euphoria on depression are frequent during treatment with corticotropin and cortisone. These minor mood disturbances are readily reversible, disappearing rapidly after the medication is discontinued. Increased tension, irritability, excitedness, facetiousness, fearfulness, and insomnia are frequently associated with these

mild mood disturbances but disappear as rapidly. In certain instances the psychological changes may reach psychotic proportions. The widespread physiological effects of corticotropin and cortisone suggest that the mood disturbances are due to altered physiological mechanisms as well as to psychological mechanisms. Four illustrative cases are described. Case 1 represented a toxic psychosis due primarily to corticotropin, with a release of underlying prepsychotic personality trends. Case 2 illustrated a toxic psychosis in which toxic elements were not prominent but in whom the toxicity precipitated or hastened the development of an unsuspected paranoid psychosis. Case 3 demonstrated a toxic state due to the drug, but great disappointment in its lack of effectiveness was probably an equally potent precipitant for the subsequent illness. In case 4 the disappointment in the effectiveness of the drug led to the recurrence of an illness she had previously experienced. The authors stress that in the management of the patient who is undergoing therapy with these powerful metabolic agents, the physician should be alert to both the toxic manifestations of the drug and the psychological circumstances under which the drugs are administered.

Journal of Applied Physiology, Washington, D. C.

4:873-934 (June) 1952

Relationship of Oxygen Tension to Hemoglobin Oxygen Saturation in Arterial Blood of Normal Men. C. J. Lambertsen, P. L. Bunce, D. L. Drabkin and C. F. Schmidt.—p. 873.

Physics of Vibrations in Living Tissues. H. E. von Gierke, H. L. Oestreicher, E. K. Franke and others.—p. 886.

Effect of Attitude of Breathing Upon Tidal Volume. L. F. Peltier and M. B. Visscher.—p. 901.

Pain Reaction to Locally Applied Heat. F. B. Benjamin.—p. 907.

Effects of Hard Competitive Muscular Work on Electrolyte Content of Thermal Sweat. K. L. Ahlman, O. Eränkö, M. J. Karvonen and V. Leppänen.—p. 911.

Instantaneous Distribution of Electrocardiographic Potential on Body Surface of Normal Man During the T Interval. R. S. Sikand, A. Mauro and L. H. Nahum.—p. 916.

Journal of Bacteriology, Baltimore

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Studies on Antibiotic Synergism and Antagonism: Synergism Among Seven Antibiotics Against Various Bacteria in Vitro. E. Jawetz, J. B. Gunnison, J. B. Bruff and V. R. Coleman.—p. 29.

Effect of Penicillin on Genetic Changes and Temporary Modifications in Populations of Brucellae. W. Braun, M. Kraft, D. D. Mead and R. J. Goodlow.—p. 41.

Effect of Ultraviolet Radiation on Production of Urease by Proteus Vulgaris and Proteus Mirabilis. G. H. Bornside, R. C. Cleverdon and W. L. Kulp.—p. 63.

Cultivation of Coccidioides Immitis in Embryonated Hen's Egg. R. A. Vogel and N. F. Conant.—p. 83.

Sulfur Metabolism in Escherichia Coli: IV. Influence of Nonmethionine Sulfur Compounds upon Methionine Requiring Mutant. D. B. Cowie and E. T. Bolton.—p. 87.

Effects of Calcium on Proliferation of Lactic Streptococcus Bacteriophage. N. N. Potter and F. E. Nelson.—p. 105.

Studies on Phagocytosis: Determination of Blood Opsonin for Brucella. J. Victor, A. D. Pollack, R. Raymond and J. R. Valliant.—p. 121.

Journal of Experimental Medicine, Baltimore

96:107-186 (Aug.) 1952

Formation of Collagen Fibers by Action of Heparin on Soluble Collagen: Electron Microscope Study. T. G. Morrione.—p. 107.

Influence of Diet on Iron Absorption: III. Comparative Studies with Rats, Mice, Guinea Pigs, and Chickens. D. M. Hegsted, C. A. Finch and T. D. Kinney.—p. 115.

Intracellular Distribution of Lansing Poliomyelitis Virus in Central Nervous System of Infected Cotton Rats. C. E. Schwerdt and A. B. Pardee.—p. 121.

Multiplication of Tubercle Bacilli Within Normal Phagocytes in Tissue Culture. E. Suter.—p. 137.

Relation of Herpes Virus to Host Cell Mitochondria. W. W. Ackermann and H. Kurtz.—p. 151.

Experiments on Cause of Rabbit Carcinomas Derived from Virus-Induced Papillomas: II. Loss by Vx2 Carcinoma of Power to Immunize Hosts Against Papilloma Virus. P. Rous, J. G. Kidd and W. E. Smith.—p. 159.

Complement-Fixing Antibodies to Type 2 (Lansing) Poliomyelitis Virus in Normal Population of Subtropical Area. N. Goldblum and J. L. Melnick.—p. 175.

Journal-Lancet, Minneapolis

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Drainage Method for Duodenal or Pancreatic Fistulae. O. F. Noel, R. S. Martin Jr. and L. C. Powell.—p. 317.

History of Blood Transfusion. A. J. Kremen.—p. 319.

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72:353-398 (Aug.) 1952

Practical Scheme for Treatment of Urinary Tract Infections. C. D. Creevy.—p. 353.

Medullary Nailing of Femoral Shaft Fractures. G. M. Hart.—p. 357.

Observations and Therapy of Peptic Ulcer in Young Adults. J. R. Fox.—p. 361.

Diagnostic Criteria for Coronary Arteriosclerotic Heart Disease. J. M. Barker and W. M. Yater.—p. 364.

Penicillin Suppositories in Abdominal and Vaginal Hysterectomies. W. W. Nelson.—p. 370.

Journal of Urology, Baltimore

68:1-412 (July) 1952. **Partial Index**

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*End Results Following Nephrectomy in Patients with Hypertension. W. F. Braasch.—p. 6.

Hypertension Due to Thrombosis of Renal Artery: Report of Case in Which Cure Was Obtained by Nephrectomy. W. F. Owen Jr. and C. K. Pearlman—p. 11.

Renal Bisection. G. W. Slaughter.—p. 17.

Radical Nephrectomy for Neoplasm. F. E. B. Foley, W. P. Mulvaney, E. J. Richardson and I. Victor.—p. 39.

Retroperitoneal Encysted Hematomas. R. Leake and T. B. Wayman.—p. 69.

Role of Infection in Nephrolithiasis. G. Carroll and R. V. Brennan.—p. 88.

*Dissolution of Urinary Calculi. H. I. Suby.—p. 96.

Etiology and Prevention of Renal Calculi. C. C. Higgins.—p. 117.

Primary Amyloidosis of Renal Pelvis and Ureter: Report of Case. L. W. Gilbert and J. R. McDonald.—p. 137.

Triplication of Ureter and Renal Pelvis. R. D. Gill.—p. 140.

Use of Plastic (Polyethylene) Tubing in Surgical Management of Ureteropelvic Obstructions. F. C. Schlumberger and P. P. Riparetti.—p. 158.

Ureteral Injury by Transurethral Electroresection and Coagulation. J. P. Davis.—p. 168.

Urologic Complications of Cancer of Uterine Cervix. E. W. Beach.—p. 178.

Use of Segments of Small Intestine as Ureters. D. W. McLean and O. G. Fais.—p. 190.

Subtotal Cystectomy for Atomic Bladder. R. J. Fitzpatrick, L. M. Orr, J. C. Hayward and J. B. Glanton.—p. 206.

*Evaluation of Hormonal Therapy in Cryptorchidism. C. L. Deming.—p. 354.

End Results of Nephrectomy for Hypertension.—Braasch reviewed 100 cases in which nephrectomy had been performed for hypertension at least two years before; in 60 cases the operation had been performed five or more years before. The blood pressure returned to normal or was significantly reduced in 64% of cases in which the patients were traced from two to five years and in 53% of cases in which the patients were traced from five to nine years following operation. These results should eliminate any doubt as to whether a unilateral renal lesion can cause hypertension and whether removal of the diseased kidney can cause the blood pressure to return to normal. Careful selection of patients for nephrectomy is essential for good results. Evidence of a lesion in the other kidney, advanced age, unsatisfactory general condition, or long duration of hypertension are contraindications to operation. Pathological conditions of the kidney that are most frequently observed in association with hypertension are atrophic pyelonephritis, hydronephrosis with infection, and renal tuberculosis. In some cases, however, the blood pressure may drop to normal following nephrectomy, with symptomatic improvement, and then gradually return to higher levels, with recurrence of symptoms after an interval of from several months to years. In such cases it is possible that nephrosclerosis existed in the supposedly normal kidney or that a dormant essential hypertension existed, with the infected kidney acting as an immediate stimulant. Removal eliminated this stimulus temporarily but hypertension subsequently may assert itself.

Dissolution of Urinary Calculi.—Much work has been done in an attempt to find an efficient yet safe method for dissolving urinary stones, but the solutions thus far prepared are still impractical in most cases. The stone is supposedly in equilibrium with the solution in which it is immersed. The theoretical principle of stone dissolution is to cause increased ionization of the stone. Stone ions, adrift in the solution can be captured by other appropriate ions, yielding a soluble product and thus forcing the stone to give more and more ions and dissolve. The importance of the index of irritation of the dissolving solution is discussed, and it is pointed out that certain solutions can be rendered less irritating by the addition of magnesium. The author also made experiments with certain water softeners and with wetting agents. After commenting on the mechanics of irrigation, he briefly presents seven cases in which irrigation was tried with a solution, but the procedure proved too painful in most cases.

Hormonal Therapy in Cryptorchidism.—Deming feels that after 25 years of prescribing and using hormones for the treatment of cryptorchidism, evaluation of this therapy is desirable. He feels that it is not advisable to wait until puberty before transplanting the testis into its natural location when nature intended its transplantation 14 years earlier. He has not been successful in treating adults by hormonal means alone. The testis must lie in the scrotum to develop to its fullest physiological extent, and it should occupy this position a number of years before adolescence. Treatment should begin before the child is aware of his deformity. Not all cases of cryptorchidism are suitable for hormonal treatment; it is contraindicated in boys with an ectopic testis or an accompanying large hydrocele or hernia. The most favorable conditions exist when the testis lies in the inguinal canal and cannot be forced into the scrotum or when there is a bilateral cryptorchidism whether or not the testes can be palpated. Hormonal treatment is rarely successful in unilateral cryptorchidism. The author found chorionic gonadotropin the most effective hormone preparation for the treatment of cryptorchidism (250 international units, given intramuscularly three times a week for a total of 3,000 units). Optimum age is the fifth year. The testis descended with hormonal therapy alone in 10 of 189 cases of cryptorchidism. Agenesis of one testis was present in 9 of the 201 surgically treated undescended testes. Orchiectomy was required in 12 cases because of short vessels or a deformed organ, but only one of these patients had been subjected to preoperative hormonal therapy and that one inadequately. The main use of chorionic gonadotropic hormone is as an adjunct to surgery.

Kansas Medical Society Journal, Topeka

53:325-368 (July) 1952

Low Transverse Incision for Pelvic Operations. M. A. Rabe.—p. 325.
Needle Biopsy of Liver as Aid in Diagnosis of Malignant Tumors. R. T. Cotton and S. Zelman.—p. 328.
Cardiac Arrest: Its Diagnosis, Etiology and Treatment. P. H. Lorhan and W. E. Swartz.—p. 332.

53:369-408 (Aug.) 1952

*Marie-Strümpell Arthritis (Including a Survey of 41 Cases Treated with X-Ray). C. M. White.—p. 369.
Psychiatry in a University Health Service. S. Gundle.—p. 373.
Acute Traumatic Subdural Hematoma: Report of Case with Slight Trauma from Boxing. C. W. Hall, D. E. Eckart, M. E. Nunemaker and R. A. Crawford.—p. 377.
Nephroptosis. A. R. Sugg.—p. 379.

Marie-Strümpell Arthritis Treated with X-Rays.—Marie-Strümpell arthritis which is also designated by such terms as rhizomelic spondylitis, rheumatoid spondylitis, and spondylarthritis, is a painful disease of unknown etiology, producing rigidity of the spine. There are remissions and exacerbations, and, as the disease progresses, bony fusion occurs. Marie-Strümpell arthritis responds well to x-ray therapy while rheumatoid arthritis shows little response to it. Treatment that relieves pain and muscle spasm is helpful in the early stages of the disease. Cortisone recently produced dramatic improvement, but symptoms usually recur after the hormone treatment is stopped. In one case with severe pain, the authors were able to control the symptoms with cortisone until the effect of x-ray treatment became manifest. Surgical orthopedic measures may be needed after there is fusion of the spine. Lumbar osteotomy corrects the flexion of the lumbar spine, allowing the patient to stand erect again. Roentgen therapy is the treatment of choice in early and in moderately advanced cases. A diagram illustrates the four spinal portals used in irradiation. Two areas are usually treated with 150 r each at each session, and each portal is usually treated three times. If symptoms are localized to the sacroiliac joints, the authors treat only this area and the lumbar spine. Usually there are symptoms referable to the entire spine. If no relief is obtained after a second series of treatments additional irradiation is usually of no benefit. The authors employed irradiation in 41 cases during the last four years. Cases treated during the last six months were not considered in the follow-up. Twenty-one patients reported good remissions lasting from one to four years, and in nine of these the remissions have already lasted for more than three years. Exacerbations may be controlled by additional roentgen irradiation.

Maryland State Medical Journal, Baltimore

1:315-366 (July) 1952

Problems of Practice. W. E. Gallie.—p. 315.
Problem of Jaundice in General Surgery. H. K. Gray.—p. 322.
Medicine's Number One Problem. H. A. Rusk.—p. 331.

Metabolism, New York

1:101-196 (March) 1952

Practical Use of Various Insulins in Management of Diabetes Mellitus. G. G. Duncan.—p. 101.
Clinical Experiences with Iodinated Thiouracil Compound: Review with some Additional Observations. M. G. Goldner and S. Kirschenfeld. —p. 111.
Hereditary Periodic Paralysis. I. Effects of Various Induced Changes in Physiological State on Paralytic Attacks. M. R. Ziegler and I. McQuarrie.—p. 116.
Id.: II. Effects of Fasting and of Various Types of Diet on Occurrence of Paralytic Attacks. I. McQuarrie and M. R. Ziegler.—p. 129.
Lack of Effect of Testosterone Propionate on Body Weight of Rats During Protein Depletion and Repletion. E. Geiger and I. El Rawi. —p. 145.
Isotopic Study of Type III Porphyrins and Hemoglobin Metabolism in Unusual Case of "Mixed" Porphyria. P. T. Lowry, V. Hawkinson and C. J. Watson.—p. 149.
Relationship of ACTH and Cortisone to Serum Lipoproteins and Atherosclerosis in Humans. B. Bloom and F. T. Pierce Jr.—p. 155.
Relationship of ACTH and Cortisone to Serum Lipoproteins of Rabbit. F. T. Pierce Jr. and B. Bloom.—p. 163.
*Effect of ACTH, Cortisone and Progesterone on Patients with Chronic Hepatic Disease. W. P. Havens Jr., R. M. Myerson and I. N. Carroll. —p. 172.
Excretion of Catechol Amines During Administration of ACTH, Cortisone and Desoxycorticosterone Acetate. R. Luft and U. S. von Euler. —p. 179.

Steroid Hormones in Chronic Hepatic Disease.—Imbalance between androgens and estrogens in many patients with hepatic disease as well as increasing knowledge of the role of the liver in the metabolism of the various steroids has stimulated interest in the effects of certain of these substances on such patients. During recent studies on chronic hepatic disease Havens and associates studied (*a*) the effect of corticotropin and cortisone on the capacity of patients with chronic hepatic disease to produce antibody and (*b*) the metabolism of progesterone in such patients as measured by the urinary excretion of pregnanediol during prolonged periods of treatment with progesterone. Eight patients were given 50 to 100 mg. of cortisone intramuscularly daily for from 8 to 165 days. Five patients were given 20 to 25 mg. of corticotropin subcutaneously every 6 hours for from 10 to 27 days. Six patients were given an intramuscular injection of 100 mg. of progesterone daily for from 24 to 30 days. Most patients were kept at modified bed rest and received a high caloric diet. Corticotropin and cortisone at best produced only temporary improvement, evidenced by a greater sense of well-being. With occasional exceptions, the changes in hepatic function and in the general condition could not be distinguished from those that might have resulted from the rest and the dietetic treatment. Untoward effects, including augmented retention of fluid, psychosis, alteration in glucose tolerance tests, coma and death, reemphasize the hazards involved in the administration of corticotropin and cortisone to patients with hepatic disease.

New England Journal of Medicine, Boston

247:113-148 (July 24) 1952

The Clinical Trial. A. B. Hill.—p. 113.
Acute Perforated Peptic Ulcer: Criteria for Operation and Analysis of 500 Cases. S. Mikal and W. R. Morrison.—p. 119.
Chronic Idiopathic Hypertrophic Osteoarthropathy: Report of Case and Review of Literature. M. Berk.—p. 123.
Hospital Administration. N. W. Faxon.—p. 127.

247:149-190 (July 31) 1952

*Congenital Absence of Right Pulmonary Artery: Diagnosis by Angiocardiography, with Cardiorespiratory Studies. I. M. Madoff, E. A. Gaensler and J. W. Strieder.—p. 149.
Electrolyte-Balance Studies in Normal Volunteers and Clinical Observations on Effects of Cation-Exchange Resins in Patients with Cardiovascular Disease and in Subjects Receiving Pituitary Adrenocorticotrophic Hormone (ACTH). C. D. Bonner.—p. 158.
Management of Bronchial Asthma. H. B. Tillman.—p. 163.
Review of Clinical Ballistocardiography. E. Rubenstein.—p. 166.

Congenital Absence of Right Pulmonary Artery.—Congenital absence of a main branch of the pulmonary artery in the presence of aerated lungs has been reported in only nine cases collected from the literature since 1868. Of these nine cases, the absence of the right branch of the pulmonary artery was recognized at postmortem examination in six, while the absence of the left branch of the pulmonary artery in the remaining three was recognized at necropsy in one, and at surgical intervention in two. Absence of the right branch of the pulmonary in a patient with apparently normal lungs has, therefore, never been recognized during life. This diagnosis was made by the authors by angiography in a 14-year-old girl who was entirely well. Physical examination and the usual laboratory studies were negative. The chest roentgenogram showed some deviation of the trachea to the right, and the right hemithorax was slightly smaller than the left. Bronchoscopy and bronchography revealed slight narrowing of the bronchus of the upper lobe of the right lung. The possible embryologic development is discussed. Pulmonary function studies showed the maximum breathing and vital capacities, residual volume, and total lung capacity to be slightly reduced. Air flow velocities, intrapulmonary mixing, and arterial oxygen saturation were normal. The minute volume was increased both at rest and during exercise. During bronchospirometry with room air, the right lung showed normal ventilation but did not participate in oxygen uptake. As the result of induced hypoxia and supplying of room air to the left lung and oxygen to the right lung, the right lung became responsible for 18% of the total oxygen uptake. The entire output of the right side of the heart entered the left lung. By application of the Fick principle to a single lung, it was estimated that 17% instead of 1% of the cardiac output on the left entered the right lung. Therapeutic implications are considered as follows: In the authors' patient, the entire additional work of the left ventricle consisting of the "effective" and "ineffective" bronchial flow is probably not great enough to warrant pneumonectomy. Removal of the right lung might be undesirable because further distention of the left lung would result. If an anomalous peripheral arterial supply to such a lung were large enough, cardiac failure might eventually ensue, and in this case resection of the involved lung or ligation of an anomalous arterial supply might prove life-saving. With this in mind the patient has been subjected to follow-up examinations at regular intervals, although at present she does not show clinical evidence of cardiac embarrassment. In three of the previously recorded cases hemorrhage into the parenchyma of the abnormally supplied lung was described. If hemoptysis should occur in the authors' patient, it may well be an indication for exploratory thoracotomy.

Oklahoma State Medical Assn. J., Oklahoma City

45:239-272 (July) 1952

Carcinoma of Cervical Stump: (Plea for Early Diagnosis and Prevention). G. Rogers.—p. 241.
Method of Management for Infertile Couple. W. C. Lindstrom.—p. 244.
The Patella—Basic Considerations. D. H. O'Donoghue and M. B. Hays.—p. 248.
Recent Advances in Surgery. A. R. Wiley.—p. 251.

Psychoanalytic Quarterly, Albany, N. Y.

21:295-464 (July) 1952. **Partial Index**

Phobic Symptoms and Dream Interpretation. B. D. Lewin.—p. 295.
Genesis of Antisocial Acting Out in Children and Adults. A. M. Johnson and S. A. Szurek.—p. 323.
Repression and Electroencephalogram. H. I. Harris.—p. 402.

Psychoanalytic Review, Albany, N. Y.

39:213-308 (July) 1952

Psychosomatic Problems: Methodology, Research Material and Concepts. P. H. Hoch.—p. 213.
Structural Aspects of Psychotherapy. R. Ekstein.—p. 222.
Thematic Apperception Test of Schizophrenic Interpreted According to New Rules. Z. A. Piotrowski.—p. 230.
Fantasies Concerning Convulsive Therapy. L. B. Boyer.—p. 252.

Psychosomatic Medicine, New York

14:243-336 (July-Aug.) 1952

Relationship of Specific Attitudes and Emotions to Certain Bodily Diseases. W. J. Grace and D. T. Graham.—p. 243.
Psychometric Investigation of Relationship Between Emotional Repression and Occurrence of Psychosomatic Symptoms. A. H. Frankle.—p. 252.
Autonomic Response Specificity and Rorschach Color Responses. J. I. Lacey, D. E. Bateman and R. Van Lehn.—p. 256.
"Psychosomatic" Phenomena in Animals. F. A. Beach.—p. 261.
Program of Teaching a Psychodynamic Orientation to Resident Physicians in Medicine. S. Kligerman.—p. 277.
Effects of SKF 7501 (N-9-Fluorenyl N, N-Ethyl-Beta-Chloroethylamine) on Cardiovascular Manifestations of Hypoglycemia Following Administration of Insulin. E. Meilman and M. D. Altschule.—p. 284.
Some Psychodynamic Considerations of Psychosomatic Skin Disorders: Plethysmographic and Psychoanalytic Observations. F. Deutsch.—p. 287.
Dermatitis: Hysterical Conversion Symptom in a Young Woman: Psychosomatic Conference. J. Barchilon and G. L. Engel.—p. 295.
Psychological Reactions to Cortisone: Clinical Note. M. H. Hollender.—p. 306.
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Radiology, Syracuse, N. Y.

59:1-160 (July) 1952

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Design and Construction of Multicurie Cobalt Teletherapy Unit: Preliminary Report. L. G. Grimmett, H. D. Kerman, M. Brucer and others.—p. 19.
Acute Miliary Diseases of Lung. B. Felson.—p. 32.
Partial Obstruction of Small Intestine: with Special Reference to Obstructing Segment. J. F. Martin and H. L. Friedell.—p. 49.
Primary Pneumaturia, with Report of Two Cases. S. Fineman, W. L. Ferber and D. N. Roginsky.—p. 63.
Glomus Jugularis Tumor of Middle Ear: Case Report. R. N. Land.—p. 70.
Roentgenography of Fibroadenoma of Breast. J. Gershon-Cohen and H. Ingleby.—p. 77.
Errors of Diagnosis in Mass Radiography. L. E. Powers and W. S. Lainhart.—p. 88.
Roentgen Study of Effect of Total Pancreatectomy on Stomach and Small Intestine of Dog. J. F. Weigen, E. P. Pendergrass, I. S. Ravdin and T. E. Machella.—p. 92.
*Effect of Radiation Dosage on Results in Carcinoma of Cervix. E. C. Porter and L. K. Sycamore.—p. 103.
Intravenous Pyelography as Aid in Classification of Carcinoma of Cervix. R. Rosh and P. Strax.—p. 107.

Radiation Dosage in Carcinoma of Cervix.—All but two of the 113 patients with carcinoma of the uterine cervix discussed in this paper received radiation therapy; these two were subjected to hysterectomy. In estimating the five-year survivals, the irradiated patients were divided into two groups, one being treated before 1940 and the other one from 1940 to 1944, inclusive. Early in 1940 the irradiation treatment was greatly changed. The roentgen ray doses administered with the new apparatus introduced at that time were considerably larger, and radium applications were given in conjunction with the roentgen treatment. This improvement in technique and the larger dosage increased the five-year survival rate from 23 to 48%. The five-year survival for the entire group was 34%.

Surgery, St. Louis

32:1-160 (July) 1952

Esophagitis After Esophagogastric Anastomosis. H. R. Ripley, A. M. Olsen and J. W. Kirklin.—p. 1.
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Study of Intestinal Intubation Using Flexible Stylet with Controllable Tip. G. A. Smith.—p. 17.
Arteriovenous Fistula of Lung Treated by Dissection and Excision Without Pulmonary Excision. E. F. Parker and J. M. Stallworth.—p. 31.
Effect of Pregnancy on Tensile Strength of Healing Laparotomy Wounds in Rats. S. A. Localio and J. L. Chassin.—p. 39.
*Acute Progressive Unrelenting Renal Failure: Manifestation of Severe Shock Associated with Upper and Lower Nephron Nephrosis. E. E. Muirhead and J. A. Stirman.—p. 43.
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Experimental Ascites—Its Production and Control. J. K. Berman and J. E. Hull.—p. 67.
Construction of Fresh Autogenous Arterial Grafts: I. Use of Splenic Artery to Bridge a Gap in Aorta. E. S. Hurwitt and A. Kantrowitz. —p. 76.
Production of Chronic Gastric Hypervagotonia. R. N. Watman and E. S. Nasset.—p. 89.
Gastrojejunal Ulcer: 10-Year Study. V. A. Weinstein and R. Colp.—p. 96.
Postoperative Pain; Its Use in Comparative Evaluation of Analgesics. E. M. Papper, B. B. Brodie and E. A. Rovensteine.—p. 107.

Acute Progressive Renal Failure.—There are several clinical types of acute renal insufficiency due primarily to tubular damage, which Lucke designated as lower nephron nephrosis. The authors describe 10 cases of acute, progressive, tubular nephropathy, with postmortem findings in 8 cases. The renal failure became apparent following prolonged peripheral circulatory failure. Shock had been present for from 6 to 48 hours. Eight patients experienced blood loss, either as a result of trauma or operative procedures; four of these in addition had received at least 500 cc. of incompatible blood. Another patient had a fulminant hemolytic anemia accompanied by hemoglobinemia and hemoglobinuria. All patients had oliguria. Hypertension was a common feature, and mental disturbances occurred regularly. Respiratory distress was severe in five patients, all of whom had pulmonary edema. Anemia became more pronounced as the uremia progressed. Terminally, the blood pressure dropped to hypotensive levels, the respiratory distress became aggravated, a comatose state ensued, and the patient succumbed gradually. Three patients had terminal convulsive seizures. At postmortem examinations the kidneys revealed involvement of the entire tubule, that is, an upper and lower nephron nephrosis, but regeneration was well advanced when death supervened. The brain and the liver displayed changes indicating advanced peripheral circulatory failure. The renal failure differed in several respects from the recoverable form of "lower nephron nephrosis." The oliguria was extreme for intervals up to 22 days, the azotemia was high and fixed, and acidosis was severe and difficult to combat. In addition, there was hypertension, diarrhea, mental aberrations, respiratory distress, and anemia. It appears plausible to consider the shock as the cause of the widespread tissue injury, including the nephropathy, the cerebral, hepatic, and possibly, to a certain extent, the pulmonary damage. The question remains whether the shock was the main lethal factor or whether uremia by itself or in combination with shock was the main cause of death.

Wisconsin Medical Journal, Madison

51:663-742 (July) 1952

*Roentgen Therapy in Pituitary Adenomas with Special Consideration of Chromophobe Type. H. M. Aitken and E. A. Pohle.—p. 666.
Secondary Abdominal Pregnancy of Five Months Duration Terminated by Laparotomy. J. A. Klieger and J. R. Evrard.—p. 672.
Reformed Mealtime Schedule: Its Effect on Weight and Serum Glucose of Tuberculous Children. K. E. Kassowitz.—p. 674.
*Hodgkin's Disease of Stomach. A. S. Jackson and E. B. Schnell.—p. 679.
Signs and Symptoms of Certain Anxiety Reactions. O. O. Meyer.—p. 684.

Roentgen Therapy of Pituitary Adenomas.—In the 15 year period ending in 1951 36 patients with pituitary tumors were observed. Seven of the 14 histologically verified tumors were chromophobe adenomas, five were malignant adenomas, one was a craniopharyngioma, and one an adamantinoma. In 12 of the 22 clinically diagnosed cases the tumors were chromophobe adenomas, in 8 eosinophilic adenomas, in 1 a basophilic adenoma, and in the remaining case the nature of the tumor remained undetermined. Thus 19 of the 36 tumors were chromophobe adenomas. Three of the 14 surgically treated patients died postoperatively, and the other 11 received postoperative irradiation. Seventeen patients received only x-ray treatment, and 5 patients received no treatment. The authors treat most pituitary tumors with an x-ray beam generated at 175 kv. filtered through 0.5 mm. Cu plus 1.0 mm. Al; the half value layer is 1.05 mm. of copper. The tumor area is cross-fired through one frontal and two temporal fields measuring 4 by 4 cm. or 6 by 6 cm. The target-skin distance is 50 cm. Ordinarily 100 to 200 r, measured in air, are administered daily to each of the three fields until a total tumor dose of between 2,000 and 3,000 r has been delivered. The first two or three treatments are given cautiously and in reduced amounts to avoid the possibility of suddenly increasing the intracranial pressure through radiation hyperemia. As an added precaution, the visual fields are checked frequently during treatment, and any pronounced contraction is an indication to suspend or reduce treatment at once. If the field contraction persists or increases, immediate surgical intervention is indicated to relieve the pressure on the optic tracts. The authors feel that x-ray therapy has a definite place in the treatment of pituitary tumors, especially postoperatively in those with incomplete removal of the tumor, but also in some cases as a single therapeutic agent. Recent experience has demonstrated that chromophobe adenomas are not as radioresistant as has been believed. Satisfactory response may be expected in these cases provided large enough doses are administered.

Hodgkin's Disease of Stomach.—Although Hodgkin's disease is usually widespread, it may occur in isolated organs. This paper describes two new cases in which it was localized in the stomach. In the first patient, a 58-year-old man, the symptoms suggested carcinoma of the cardia. At operation an extensive tumor of the greater portion of the stomach was found. The lymph nodes in the greater omentum and periaortic region were enlarged. A high, subtotal gastrectomy was performed with an anterior gastrojejunostomy of the Hoffmeister type. The patient was discharged after an uneventful recovery. He received follow-up deep x-ray therapy. Microscopic examination of the stomach lesion was not characteristic of Hodgkin's disease, but the lymph nodes gave a more clear-cut picture. They showed partial to complete loss of the normal architectural pattern. Only a few well-circumscribed foci of lymphocytes remained. The large Sternberg-Reed cells were numerous. Plasmocytes and eosinophils were widely distributed throughout the nodes. After discharge the patient continued to gain weight and strength. The second patient, a 53-year-old man, complained of dull, aching, epigastric pain of four months' duration. Laparotomy revealed a mass about 3 by 1 in. (7.6 by 2.5 cm.) in size on the greater curvature of the stomach, and on the lesser curvature a smaller mass appeared to be inflammatory. The stomach was opened, and an ulcer was found in each of the masses. Small, firm lymph nodes were present in both the lesser and greater omentum. A partial gastric resection was done, with a gastrojejunostomy of the Hoffmeister technique. The patient made an uneventful recovery and received follow-up deep x-ray therapy. The pathological diagnosis was malignant lymphoma of the stomach. From the histological appearance of the lymph nodes it was classified as Hodgkin's disease. Since localized Hodgkin's disease of the stomach is generally diagnosed as carcinoma, the patients will usually come to operation. Even if the diagnosis is suspected, the patient should be treated surgically as in carcinoma of the stomach. If the lesion is inoperable, a biopsy should be taken. The patient should be given the benefit of roentgen therapy in case he has Hodgkin's disease instead of carcinoma. The use of nitrogen mustard may also prolong the life of these patients.

FOREIGN

Acta Chirurgica Scandinavica, Stockholm

103:165-240 (No. 3) 1952. **Partial Index**

*Abdominal Aortography, with Special Reference to Renal Diagnosis. A. Palmlöv.—p. 165.
*Routine Cholangiography at Operations for Gallstones. J. Swedberg. —p. 175.
Analysis of Surgical Material of Thyrotoxicosis. Y. Edlund and T. Von Schreeb.—p. 194.
Diffuse Papillomatosis in Rectum: Report of Five Cases. B. Snellman. —p. 205.
Post-operative Recurrence of Lumbar Disk Herniation. T. Törma.—p. 213.
Effect of Treatment of Traumatic Wounds with Soap Solution: Experimental Study. B. Falconer, S. Liljedahl and T. Olovson.—p. 222.

Abdominal Aortography and Renal Diagnosis.—Palmlöv performed abdominal aortography on 42 patients with urologic disorders. He used the technique described by Dos Santos and associates in 1937, in which 30 cc. of contrast solution is injected rapidly (in 5 to 6 seconds) with a syringe or a pressure apparatus. No traction or pressure should be exerted on the tube-needle connection during the injection, for this may result in dislocation of the needle and para-aortic injection. This occurred in a few of Palmlöv's cases. General or spinal anesthesia was used in all instances, but the examination may also be performed under local anesthesia. All patients had been previously examined with intravenous urography, and the majority also with retrograde pyelography. Abdominal aortography provided more extensive information than previously employed methods in 19 cases, confirmation but not additional information in 14 cases, and no information in 9 cases. No serious complications resulted. The method not only visualized the renal vessels but also the excretory cells and channels. This was of considerable diagnostic value. The best results were obtained in the diagnosis of malignant renal tumors and renal anomalies. In cases where no excretion is obtained from one kidney in intravenous urography and retrograde pyelography is impossible, abdominal aortography may be of great diagnostic value. Aortography was tried for estimation of renal function in cases of hydronephrosis and ureteral occlusion from tumor. The results were encouraging but not conclusive.

Cholangiography During Gallstone Operations.—A review of 700 cases in which cholangiography was used during operation for gallstones revealed that no complications could be traced to cholangiography. After introduction of routine cholangiography, the frequency with which stones were found in the common duct increased from 8.5% to 16.0%. In 22 cases stones in the common duct would have been missed if cholangiography had not been done. In 77 cases choledochotomy would have been done if cholangiography had not revealed that the duct was patent and free of stones. The frequency of postoperative complications was higher among the patients who had been subjected to choledochotomy than among those in whom such intervention could be avoided, and repeated cholangiography was not accompanied by an increase in the frequency of complications. Swedberg feels that cholangiography should be done at all operations for gallstones and that it is probably not contraindicated by coexistent cholecystitis, cholangitis, or pancreatitis.

Acta Dermato-Venereologica, Stockholm

32:265-354. (No. 4) 1952. **Partial Index**

Studies on Role of Lymphocytes in Antibody Production. T. Wesslen. —p. 265.
Allergic Cutaneous Vasculitis. M. Ruiter.—p. 274.
Generalized Dermatitis and Acute Lethal "Syphilitic" Pneumonia Due to Allergic Reaction to Arsphenamine. H. N. Hadders and C. T. B. Wakkerman.—p. 289.
Pharmacologic and Pathogenetic Effects of Mepacrine Chloride (Atabrine) Upon Human Skin. F. Herrmann and O. B. Miller.—p. 304.
*Lupus Erythematosus Disseminatus: Four Cases Treated with ACTH. L. M. Sonne and M. Schwartz.—p. 333.

Corticotropin in Disseminated Lupus Erythematosus.—Until recently treatment of disseminated lupus erythematosus was purely symptomatic, and the disease was usually fatal within an average of 18 months. Reports about the use of corticotropin indicate that, while the immediate effects have been good, symptoms usually recur as soon as the corticotropin therapy is stopped, although one case has been reported in which there were no symptoms for two months after treatment had been stopped. Although cure of disseminated lupus erythematosus cannot be expected, the authors felt that the poor prognosis with symptomatic treatment justifies the use of corticotropin. They describe four cases in which they resorted to treatment with corticotropin. In three of the four patients the symptoms disappeared within a few days, but the treatment had to be resumed, as all three patients relapsed. The fourth patient, who was moribund, showed no definite clinical effect, but characteristic changes were observed in the blood. The increased hormonal excretion during treatment was less marked in this case than in the others. In three cases, the treatment was accompanied by a decrease in the hyaluronic acid of the skin and by a decrease in the effect of the blood on antihyaluronidase prepared from bovine testes. In all four patients a marked depression of the elevated serum globulin was observed. Two of the patients died; the other two are still living but are not cured.

Arquivos de Neuro-Psiquiatria, São Paulo

10:125-258 (June) 1952. **Partial Index**

Early Diagnosis of Parkinsonism. R. Wartenberg.—p. 139.
Erythralgias and Their Physiopathological Aspect. R. Bing.—p. 147.
Clinical Forms of Intracranial Arterial Aneurysms. A. H. Schroeder and A. Schroeder Otero.—p. 165.
Carotid-Cavernous Fistula. B. J. Alpers.—p. 203.
*Multiple Sclerosis Appearing Clinically as a Cervical Medullary Syndrome with Slowly Progressive Evolution for 16 Years. L. Barraquer-Bordas and J. M. Segarra-Obiol.—p. 247.

Multiple Sclerosis as Cervical Spinal Cord Syndrome.—A woman with atypical multiple sclerosis had symptoms suggestive of disease localized in the lower cervical spinal cord. Other atypical features were the slowly progressive character of the disease and the unusual clinical silence of the cerebral lesions. The illness began about 1935, when the patient was 42, with motor difficulty in the lower right leg. The weakness increased slowly, and finally extended to the left leg. Examination in 1936 at a neurological clinic revealed spasmodic paraplegia, with heightening of the deep reflexes, clonus, and bilateral Babinski sign. She complained of weakness in the lower limbs and pain in the spine. Fourteen years later she entered the municipal service of geriatrics, having been bedridden for some months and unable even to sit up unaided. She had no pain or paresthesia. Results of physical and neurological examinations and the history suggested a condition limited to the spinal cord; multiple sclerosis was considered, but seemed unlikely, not only because of the uninterrupted course of the disease and the apparent absence of disseminated lesions but also because there were no modifications of speech, paresthesia, nystagmus, diplopia, etc. Cervical spinal cord compression was considered, and as it was the only condition suggested for which treatment was possible, an exploratory laminectomy was undertaken. No signs of compression were found, but the cord was abnormal in color, being pale and whitish, and very finely vascularized. The dura was closed, and the wound sutured. Influenza was unfortunately epidemic at the time and on the second postoperative day bronchopneumonia developed, which ended in death in spite of massive doses of penicillin and cardiotonics. Autopsy findings of areas of demyelinization and sclerotic plaques in the central nervous system established multiple sclerosis as the correct diagnosis.

Ärztliche Forschung, Munich

6:283-334 (July 10) 1952. **Partial Index**

Alloxan Diabetes. F. Meythaler, E. Kühnlein and J. E. Lahmann.—p. 283.
New Observations on Carbohydrate Metabolism and Their Clinical Significance. O. Wieland.—p. 298.
Neuroregulation of Blood Sugar and Insulin Tolerance as Test for Sympathetic Regulation. P. Kezdi and H. Steigerwald.—p. 309.
*Insulin Dosage and Hyperlipemia as Pathogenic Factors in Retinopathy in Diabetic Patients. M. Gaida.—p. 314.

Pathogenesis of Retinopathy in Diabetes Mellitus.—Gaida points out that during the last 25 years the aim of the treatment of diabetes has been to produce, with the aid of insulin, normal blood sugar levels and to keep the urine free from sugar. During this insulin era the incidence of retinopathy has greatly increased, from 8.3% in 1921 to 30% in 1944. The insulin requirements

vary, but it has been estimated that the healthy pancreas produces about 40 units daily, and patients who have had total pancreatectomy have been maintained with from 20 to 40 units. Since many diabetic patients receive much larger doses of insulin, it is possible that the resulting insidious shocks and the depressions in the blood sugar level are contributing factors to the development of retinopathy. A high fat content of the diet, which involves hypercholesteremia, is also regarded as an essential factor in the vascular changes involved in retinopathy. A diet low in fat and cholesterol but with rather liberal amounts of carbohydrates and low dosage or complete omission of insulin might reduce the incidence of retinopathy in elderly patients with diabetes. The estimation of the insulin dosage requires particular caution in diabetic patients with sclerosis of the coronary, cerebral, or renal arteries.

British Heart Journal, London

14:309-428 (July) 1952

Acute Benign Pericarditis of Unknown Origin. D. H. Davies.—p. 309.
Cor Biloculare. M. Campbell, F. Gardner and G. Reynolds.—p. 317.
Effect of Posture on Venous Velocity, Measures with $^{24}NaCl$. H. P. Wright and S. B. Osborn.—p. 325.
Praecordial T Deflection of Electrocardiogram. A. J. Brink and J. F. Goodwin.—p. 331.
Vectorcardiogram of Cardiac Infarction. W. Brigden and J. Shillingford. —p. 339.
Persistent Ectopic Auricular Tachycardia in Children. J. D. Hay and S. E. Keidan.—p. 345.
Paroxysmal Ventricular Standstill. H. Cookson.—p. 350.
Exercise Test in Patent Ductus Arteriosus. D. Lewes.—p. 357.
Circulatory Changes in Mitral Stenosis at Rest and on Exercise. J. D. Ball, H. Kopelman and A. C. Witham.—p. 363.
Injection of Bronchial Circulation in a Case of Transposition. L. Cudkowicz and J. B. Armstrong.—p. 374.
Electrocardiographic Features of High Posterolateral Myocardial Infarction. J. A. Tulloch.—p. 379.
Tricuspid Atresia: New Radioscopic Sign. P. J. D. Snow.—p. 387.
Electrocardiographic Changes in Acute Poliomyelitis in Childhood. L. M. Rose.—p. 391.
Comparison of Different Systems of Vectorcardiography. H. C. Burger, J. B. Van Milaan and W. Den Boer.—p. 401.
Small Pulmonary Vessels in Mitral Stenosis. E. W. Henry.—p. 406.
Ventricular Weight in Cardiac Hypertrophy. R. M. Fulton, E. C. Hutchinson and A. M. Jones.—p. 413.
Heart Disease in Scleroderma. D. W. Barritt and W. O'Brien.—p. 421.

British Journal of Surgery, Bristol

39:481-586 (May) 1952. Partial Index

*Association of Chronic Ulcerative Colitis and Carcinoma of Rectum and Colon. P. B. Counsell and C. E. Dukes.—p. 485.
Significance of Level of Peritoneal Reflection in Surgery of Rectal Cancer. M. R. Ewing.—p. 495.
Epithelial Survival After Cutis Grafting. N. O. K. Gibbon and K. R. Lothian.—p. 501.
Combined Cervico-Buccal Partial Pharyngectomy for Cancer of Oropharynx. R. W. Raven.—p. 503.
Retroperitoneal Pelvic Leiomyosarcoma. L. B. Fratkin, W. Stoffman and E. Landa.—p. 506.
*Herniated Nucleus Pulposus: Free Fragment. J. E. Paterson and W. Gray.—p. 509.
Para-Iliac Nerve. F. R. Wilde.—p. 514.
Pseudotuberculoid Reaction Following Irradiation of Skin. B. B. Milstein.—p. 520.
Impacted Posterior Fracture-Dislocation of Temporomandibular Joint. B. Plewes and A. K. Mighton.—p. 522.
Case of Rhabdomyosarcoma of Thigh. P. Somerville.—p. 524.
Osteoclastoma of Skull. G. F. Rowbotham.—p. 527.
Non-Parasitic Cysts of Liver. F. E. Stock.—p. 530.
Multiple Epiphysial Dysplasia: Report of Four Cases. J. K. Watt. —p. 533.
Technique and Management of 'Hindquarter' Amputation. G. Gordon-Taylor and R. Monro.—p. 536.
Carcinomata Developing at Site of Foreign Bodies in Lung. A. H. M. Siddons and A. M. MacArthur.—p. 542.
Recurrent Carcinomata. M. Lee.—p. 545.

Chronic Ulcerative Colitis and Carcinoma.—Thirteen cases of carcinoma of the large intestine which complicated ulcerative colitis are reported. Seven of these were patients of one hospital in which 63 cases of severe ulcerative colitis were treated surgically during the same period, so that the incidence of malignancy in these cases was 11.1%. The authors deduce from this that ulcerative colitis predisposes to carcinoma. This is not widely recognized. They observed that a carcinoma following chronic ulcerative colitis may not cause a visible tumor or ulcer on the surface but may manifest itself only as a dense, fibrous-looking stricture with ill-defined boundaries, resembling an inflammatory rather than a neoplastic lesion. Furthermore, when carcinoma follows chronic ulcerative colitis, it usually grows very rapidly. In nearly all the cases the authors studied, the tumor was anaplastic, having the microscopic structure of an undifferentiated colloid carcinoma or an adenocarcinoma of a high grade of malignancy. Also these growths were exceptionally invasive in character, spreading intramurally by infiltration within the submucosa and muscle coat, well beyond the visible boundaries of the surface lesion. Lymphatic spread also occurred at an unusually early stage, and the average number of lymphatic metastases was greater than for other cases. These findings indicate a bad prognosis, which follow-up records abundantly confirmed.

Free Fragment in Herniation of Nucleus Pulposus.—In a series of 91 patients with lumbar disk lesions, 11 were found to have fragments of disk tissue between the annulus and the posterior longitudinal ligament, while in 8 others pieces of fibrocartilage had passed through the posterior longitudinal ligament and lay free within the spinal canal. In two of these a still further displacement had occurred, the ventral dura was torn, and the fragments lay within the theca. Reports of the operative findings in these eight cases are given in detail. The authors found only two other papers in which the incidence of cases with free fragments was comparable to that in their own group. This seems to be related to the selection of cases for operation, that is, the more thorough the trial of conservative treatment, the greater should be the proportion of cases like those under discussion. Most of the eight cases here reviewed showed features which, though not distinctive, might suggest that a condition other than the usual form of disk lesion was present. The commonest was a tendency to relapse. The closer the resemblance to the picture of a cauda equina tumor, the more distinct were the clinical features from those of the ordinary disk lesion. Involvement of several roots and of bladder function were such features. Operation may reveal a hole in the annulus, and the fragment must be searched for until found. In other cases, the aperture may have been sealed by the root and a free fragment may be some distance away. In still others the fragment may be missed because the symptoms had been those of an ordinary disk herniation. Free fragments might not be overlooked at operation if hemilaminectomies were done routinely.

British Medical Journal, London

2:1-52 (July 5) 1952

Banti's Disease and Splenic Anaemia: Symptomatology and Aetiology. H. Tidy.—p. 1.
Surgical Treatment of Banti's Syndrome. A. H. Hunt.—p. 4.
Symmetrical Arterial Occlusion of Upper Extremities, Head, and Neck: Rare Syndrome. E. Skipper and F. J. Flint.—p. 9.
Observations on Behaviour of Erythroblasts Cultured in Normal and "Pernicious Anaemia" Sera. E. L. Feinmann, J. Sharp and J. F. Wilkinson.—p. 14.
Norwegian Scabies. G. C. Wells.—p. 18.
Ovarian Dysfunction and Hepatocholecystopathy in Association with Retrodisplacement of Uterus. N. C. Louros and N. M. Kairis.—p. 20.
Haemoglobinuria in Case of Cholera. S. N. De, K. P. Sengupta and N. N. Chanda.—p. 22.
Massive Haemorrhage from Acute Gastric Ulcer. V. J. Downie.—p. 24.

2:53-106 (July 12) 1952

Topics, Thoughts, and Tendencies. P. T. O'Farrell.—p. 53.
Failure of Antihistamine Drug to Influence Course of Experimental Human Burns. S. Sevitt, J. P. Bull, C. N. D. Cruickshank and others.—p. 57.
Conversion of Folic Acid to Citrovorum Factor in Health and Pernicious Anaemia. G. H. Spray and L. J. Witts.—p. 62.
Use of Dehydroisoandrosterone in Psychiatric Treatment: Preliminary Survey. E. B. Strauss, D. E. Sands, A. M. Robinson and others. —p. 64.
Treatment of Inadequate Personality in Juveniles by Dehydroisoandrosterone: Preliminary Report. D. E. Sands and G. H. A. Chamberlain. —p. 66.
Treatment of Sjögren's Syndrome with ACTH. E. F. B. Cadman and A. J. Robertson.—p. 68.
Sudden Death Following Injection of Penicillin. W. O. Thomson.—p. 70.
Comparison of Vasoactive Drugs in Man. P. R. Bromage.—p. 72.
*Kartagener's Syndrome. S. Karani.—p. 74.

Kartagener's Syndrome.—The association of bronchiectasis and sinus maldevelopment with transposition of the viscera was reported by Siewert as early as 1904 and later by several other observers. The triad is now generally referred to as Kartagener's

syndrome, Kartagener having described four cases in 1933 and together with Horlacher seven additional ones in 1935. So far a total of 82 cases have been reported, some of them having occurred in twins and siblings. The hereditary and familial tendencies of the syndrome were first observed by Guenther but later were stressed also by Kartagener and others. The two cases described in this paper occurred in sisters with a family history of chest disorders. The father has chronic bronchitis and one brother, who could not be traced, was said to have a weak chest and had been told that his heart was on the wrong side. Both of the women had been subject to recurrent infections of the respiratory tract followed by chronic bronchitis or chest trouble with troublesome cough and copious, foul-smelling sputum. The frontal and sphenoidal sinuses were very small or absent. Situs inversus totalis was confirmed in both by roentgenologic examination. An interesting feature of Kartagener's syndrome lies in the possibility that a congenital defect of the bronchial wall is a primary cause of bronchiectasis. Infection of the upper respiratory tract and bronchial obstruction are usually regarded as important factors in the causation of bronchiectasis, but not all cases of bronchiectasis show evidence of both or even one of them. Moreover, Olsen in 1943 reported four cases of dextrocardia with bronchiectasis without sinus infection, and the very existence of this syndrome supports the theory that the weakness in the walls of the bronchioles is the primary factor in affecting their dilatation, perhaps aided by chronic infection.

Canadian Medical Association Journal, Montreal

67:1-92 (July) 1952

Nature of Muscular Diseases. D. Denny-Brown.—p. 1.
Alopecia Areata. K. I. Freeman.—p. 6.
Principles and Management of Postoperative Care. R. G. B. Gilbert.—p. 9.
Treatment of Tuberculous Meningitis with Cortisone and Streptomycin. S. J. Shane, R. A. Clowater and C. Riley.—p. 13.
Artificial Bile Duct. J. R. McCorriston and D. W. MacKenzie Jr.—p. 15.
Some Observations on Staphylococci and Their Resistance to Antibiotics. G. B. Leyton.—p. 20.
Psychogenic Factor in Migraine. C. J. Malloy.—p. 23.
Study of Complications Resulting from Treatment of Cancer of Cervix. N. A. McCormick.—p. 25.
Survey of Methods Used to Reveal Eye Defect in School Children. A. L. Morgan, J. S. Crawford, T. J. Pashby and J. R. Gaby.—p. 29.
The Diabetic in Industry. I. M. Rabinowitch.—p. 34.
Billroth I Gastrectomy. J. A. Barclay.—p. 41.
Spontaneous Pneumohaemothorax; Report of 3 Cases. S. L. Eidinger and E. H. Rubin.—p. 43.
ACTH, Cortisone and Tuberculosis. A. W. Capon.—p. 46.
*Adventures with Decamethonium Bromide. R. Duchesne.—p. 48.
ACTH in Treatment of Multiple Wasp Stings. E. S. James and W. G. Walker.—p. 50.

Reactions to Decamethonium Bromide. — Duchesne presents seven cases in which prolonged respiratory paralysis followed intravenous injection of decamethonium bromide (syncurine®). This agent has been used as a relaxant at the author's hospital in over 4,000 cases during the last two years. Four of the seven patients described had atrophy of the liver, two were jaundiced, and one had both jaundice and atrophy of the liver. The doses injected were considered normal. In most of these cases the only therapeutic measure was artificial respiration with oxygen. In each case, spontaneous respiratory activity was promply followed by return of consciousness. There were no ill effects. Other observers reported cases of apparent prolonged action of decamethonium bromide in which intercostal activity was greatly impaired at the end of the operation. In the patients reported on here, it is probable that the prolonged respiratory paralysis is more than a coincidence. The effects of the relaxing agent persisted longer than usual. It is not known whether decamethonium bromide is destroyed in the liver or whether in jaundiced patients there is a substance that prevents or delays its destruction.

Edinburgh Medical Journal

59:297-360 (July) 1952

Reflections from Provincial Deanery. J. G. McCrie.—p. 297.
Thirty Years' Experience of Megaloblastic Anaemais. L. S. P. Davidson.—p. 315.
Dermatomyositis: Case Report. H. G. H. Richards.—p. 327.
Retinal Changes in Hypertension. J. Macaskill.—p. 334.
Turner's Syndrome in a Male Infant. T. James.—p. 344.

Fortschr. Röntgenstrahlen & Röntgenpraxis, Stuttgart

76:691-842 (June) 1952. **Partial Index**

Roentgenologic Manifestations of Neurogenic Tumors of the Digestive Tract. R. Pape and H. A. Hackenselliner.—p. 691.
*Cytologic Studies as Aid in Diagnosis of Bronchial Carcinoma. J. H. Schaaf and G. Suchowsky.—p. 711.
*Roentgenologic Picture of Pneumonoconiosis Due to Soot. R. Töppner.—p. 722.
Roentgenologic Observations During Influenza Epidemic of 1951. K. Breckoff and V. O. B. Lohmann.—p. 728.
Changes in Position of the Heart and Their Manifestation in the Electrokymogram. K. Heckmann.—p. 744.
Clinical Aspects of Solitary Plasmocytoma. W. Boecker and M. Knedel.—p. 764.

Cytological Studies in Diagnosis of Bronchial Carcinoma.—It has been demonstrated that cytological studies on sputum or bronchial secretion permit a positive diagnosis of bronchial carcinoma in a certain percentage of cases. Reviewing the literature, Schaaf and Suchowsky found that the percentage of correctness varies between 42 and 89%. Analyzing their own material, they gained the impression that the extremely high percentages of correctness of cytological diagnoses must be regarded with skepticism. They made their studies chiefly on material withdrawn from the bronchial tree. This method is far superior to examination of the sputum. The presence of atypical cells does not permit a definite diagnosis of bronchial asthma, nor can the absence of such cells be regarded as definitely ruling out the existence of bronchial carcinoma.

Roentgenograms of Lungs of Workers Exposed to Soot.—Roentgenographic studies were made of the lungs of 334 employees of a soot factory. The studies were made in a research institute for pneumonoconiosis. It was found that soot pneumonoconiosis begins with soft streak and reticular patterns and later there are blotchy shadows of slight density. The accompanying bronchial shadows and the fact that indurations are absent or slight suggest soot pneumonoconiosis in workers with a history of exposure to soot, although they are not necessarily specific for this occupation. Only the extremely slow progression of the changes and the absence of pulmonary emphysema despite intensive exposure are characteristic of soot pneumonoconiosis. A man who had worked in a soot factory had roentgenographic evidence of soot pneumonoconiosis. Autopsy studies after he committed suicide revealed among other changes extensive adhesions between the right lower lobe and the thoracic wall and the diaphragm. Extensive deposits of soot were found subpleurally. The cut surface of the lung was almost black. The musculature of the right ventricle was of greater than normal thickness and the left ventricle showed hypertrophy. There was evidence of considerable anthracosis, and the severe pulmonary emphysema had impaired the pulmonary circulation, as indicated by the hypertrophy of wall of the right ventricle. Microscopic examination of the lung showed emphysematous dilatation of the alveoli. Many black irregular nodules were observed. The soot deposits were found especially near the arteries and bronchi.

Giornale Italiano di Chirurgia, Naples

8:301-399 (May) 1952. **Partial Index**

*Bronchoscopy and Intrabronchial Therapy in Surgical Bronchopulmonary Diseases. D. Mori.—p. 301.
Surgical Treatment of Perforated Gastroduodenal Ulcer. A. Acquati.—p. 322.

Bronchoscopy and Intrabronchial Therapy.—Bronchoscopy was performed in 537 patients for treatment of bronchial tumors, acute and chronic suppurations, and foreign bodies and for bronchial exclusion in pulmonary resection. It was a valuable diagnostic and therapeutic method in cases of bronchial tumor because it made possible histological and cytological examination of tissue, secretion, and lavage fluid bronchoscopically removed. This was the best possible material for cytological diagnosis, because it was less diluted and did not contain cells from the mouth and the pharynx. Examination of bronchoscopically removed material gave positive results in 43% of the author's cases, whereas results of cytological examination of the sputum from the same patients were positive in only 21%. Better results may

be obtained with the sponge biopsy method. In some cases a definite diagnosis was impossible, since endoscopic vision is limited only to some segments of the bronchial tree. Even in these cases bronchoscopy was valuable in revealing integrity of the vocal cords, displacement of the tracheal axis, infiltration of the mucous membrane, stenosis, and other conditions that were of help in establishing the nature, extension, and possible surgical treatment of the lesion. In recent acute suppurations intrabronchial therapy by means of aspiration, lavage, and instillation of fluids, chemotherapeutic drugs, and antibiotics gave good results and in many cases complete recovery. In chronic suppurations it reduced cough, expectoration, and temperature, and improved the patient's general condition, thus making surgical intervention easier. Results were also good when bronchoscopy was performed preoperatively to block the passage of exudate from an involved lobe or lung. It was also valuable in postoperative cases for the aspiration of secretions or blood and for the removal of foreign bodies from the lungs of two patients. When the foreign bodies are not radium-opaque, bronchoscopy also has diagnostic value. Contraindications for bronchoscopy are aneurysm of the aorta, Pott's disease, cardiac decompensation, and tuberculous, syphilitic, and neoplastic laryngitis. Complications are usually pharyngolaryngitis and small hemorrhages.

Journal of Mental Science, London

98:373-514 (July) 1952. **Partial Index**

Patients' Attitudes to Leucotomy and Its Effects. E. Stengel.—p. 382.
Lower Quadrant Leucotomy. F. T. Thorpe and J. Hardman.—p. 389.
*Cortisone in Treatment of Schizophrenia. L. Rees and G. M. King.—p. 401.
Psychiatric Aspects of Epilepsy in Children. D. A. Pond.——p. 404.
Studies on Physiology of Awareness: Oximetric Investigation of Anoxaemia Accompanying Insulin Coma Therapy. J. W. Lovett Doust and R. A. Schneider.—p. 411.
Effect of Electrical Stimulation of Brain on Perception of Pain. P. G. Croft.—p. 421.
Assessment of Pain Perception. P. G. Croft.—p. 427.
*Observations on Relation Between Insulin Coma Dosage and Prognosis in Schizophrenia. R. K. Freudenberg.—p. 441.
Treatment of Mental Defectives with Glutamic Acid. M. Foale.—p. 483.

Cortisone in Schizophrenia.—Twelve schizophrenic patients were matched in six pairs according to age, sex, clinical status, duration of illness, and previous treatment. All patients were given injections of sterile water for the first week while all of the tests were carried out. During the second week cortisone was given intramuscularly in divided doses as follows: 300 mg. on the first day, 200 mg. on the second day, and 100 mg. on the third and fourth days. Psychiatric rating scales, psychological and physiological tests such as eosinophil counts, blood pressure and water balance estimations, and electroencephalography were carried out before, during, and after the period of clinical trial. No significant improvement was noted by clinical observation or by means of psychiatric rating scales. One patient become temporarily worse during cortisone therapy and returned to his previous state afterwards. The investigation provided no evidence to suggest that cortisone given by the method described had beneficial therapeutic effects in schizophrenia.

Insulin Dosage and Prognosis in Schizophrenia.—The increased incidence of schizophrenia at puberty, which reaches its peak at 20 in men and 25 in women, and the rapid decrease after these ages has pointed to the sex steroids as an important factor in this disorder. Recent evidence on the relationship of sex hormones and insulin suggests that estrogens have a "sensitizing" and androgens a "desensitizing" effect. An investigation into the insulin sensitivity in clinically different schizophrenic groups and in the two sexes should, therefore, throw some light on other endocrinological mechanisms. The amount of insulin needed to produce a hypoglycemic coma was significantly higher in males than in females, whatever the therapeutic effect. Lower insulin coma dosages had a tendency to be correlated with a good therapeutic response. Only 14 men responded favorably and 18 unfavorably, while the corresponding figures for women were 36 and 17. Female patients in whom the schizophrenia has persisted for less than six months needed smaller doses of insulin than male patients with the same length of illness. With longer duration of schizophrenia this difference disappeared. The prognosis was better in female than in male patients. Atypical patients had the lowest minimal dosages and the best therapeutic response. Neither the body-index type nor the body weight was correlated significantly with the prognosis. The author feels that the results suggest that sex steroids could be used in combination with insulin shock therapy.

Journal of Tropical Medicine and Hygiene, London

55:145-168 (July) 1952

Infant Mortality Rates in Rural Areas in Gambia Protectorate. D. P. Gamble.—p. 145.
Observations on Minor Degrees of Anaemia in East African Workers. R. F. Tredra.—p. 149.
*Note on Fluorescence Microscopy in Diagnosis of Leprosy. M. A. Gohar.—p. 156.

Fluorescence Microscopy in Leprosy.—It is often possible to diagnose leprosy in its early stages by microscopical examination of scrapings taken from the nasal mucosa, where small lepromas are frequently found, sometimes long before their appearance on the skin. Even in the anesthetic type of the disease these lepromas are often found only at this site. For routine diagnosis, films are made from these scrapings and stained by the Ziehl-Neelsen method, but there may be so few organisms that they are missed in spite of prolonged search. The aim of the work reported here was to find out if fluorescence microscopy would increase the percentage of identifications in the examination of films for the leprosy bacillus. A comparison was made between the results obtained by staining films by the Ziehl-Neelsen method and examining them by ordinary light and by staining films with auramine and examining them by filtered ultra-violet rays and an eyepiece provided with a yellow filter. Scrapings from the nasal mucosa were taken in 23 cases of early leprosy, but when there was a tendency to bleed, swabs were taken instead. A slightly higher percentage of positives is obtained by fluorescence microscopy than by the Ziehl-Neelsen method, provided that adequate care is taken to avoid decolorization. However, because of certain difficulties this method seems to have little advantage over the Ziehl-Neelsen method.

Klin. Monatsbl. für Augenheilkunde, Stuttgart

121:1-128 (No. 1) 1952. **Partial Index**

Treatment of Herpetic Inflammations of the Cornea by Means of Dihydroergotamine. G. Gross.—p. 15.
Angiospastic Retinitis Due to Endocrine Factors (Late Sequel of Cushing's Disease). A. Nover.—p. 40.
Traumatic Impairment of Retinal Vessels in Juvenile Hypertension. R. Siebeck.—p. 46.
Changes in the Eye Ground in Besnier-Boeck-Schaumann's Disease. G. Mackensen.—p. 51.
*Argyll Robertson Syndrome and Suprasellar Tumor. H. Fanta and H. Reisner.—p. 63.

Argyll Robertson Syndrome and Suprasellar Tumor.—The Argyll Robertson phenomenon in which the pupil is miotic and does not respond to light stimulations is generally regarded as indicative of a syphilitic process. In the woman whose case is reported there was no evidence of a syphilitic process, but neurological examination suggested the presence of a suprasellar tumor. Surgical treatment corroborated this diagnosis, revealing a large, solid suprasellar tumor that histological examination revealed to be a craniopharyngioma. Complete removal of the tumor proved impossible, but the pressure on the chiasm and the optic nerves was relieved by removal of most of it. The postoperative course was uneventful. As early as one week after the operation the optic papilla had a better color and the visual acuity of the right eye was considerably improved. The pupils reacted to light, although this reaction was not as yet very extensive. The pupil became larger following the operation. Ophthalmologic examination at the end of two months showed additional improvement in the visual acuity of the right eye, the visual fields of both eyes were improved, and the patient stated spontaneously that she could see better. This case proves that the Argyll Robertson syndrome cannot be regarded as pathognomonic for neurosyphilis.

Lancet, London

2:1-48 (July 5) 1952

Reason and Unreason in Psychological Medicine. E. B. Strauss.—p. 1.
Influence of Iodine on Release of Thyroid Hormone in Thyrotoxicosis. G. Ansell and H. Miller.—p. 5.
*Effect of Induced Vascular Hypotension on Liver: Alterations in Appearance and Consistence. P. R. Bromage.—p. 10.
Effect of Hypotension-Producing Drugs on Renal Circulation. J. Mackinnon.—p. 12.
Treatment of Rheumatoid Arthritis with Butazolidine. J. P. Currie.—p. 15.
Benemid in Treatment of Streptococcal Endocarditis. G. P. Baker and T. Pilkington.—p. 17.
Haematuria From an Undetected Urachal Tumor. R. C. Begg.—p. 18.

Effect of Induced Hypotension on the Liver.—The technique of inducing hypotension during surgical procedures is sanctioned by the following argument. The level of the systemic arterial blood pressure is immaterial if there is adequate capillary circulation, which is ensured when the pressure at the arteriolar end of the capillary exceeds the sum of the venous pressure and the colloid osmotic pressure of the plasma, a total of about 32 mm. Hg in normal man. A consideration of the anatomy and physiology of the blood supply of the liver suggests, however, that a higher critical level of hypotension may be expected for the liver than for other tissues. Between this level and 32 mm., the local circulation will be deficient in the liver, in spite of adequate capillary circulation elsewhere. Bromage studied the appearance of the livers of 17 patients during upper abdominal operations under conditions of controlled vascular hypotension to find out whether any gross changes were to be seen at low blood pressures. Differential epidural block, i. e., sympathetic and sensory, but not motor, block, was induced by Dogliotti's method under thiopental and nitrous oxide with oxygen anesthesia, and the upper level of analgesia was carried to the second thoracic segment or higher. The inhaled gases were delivered through a large-bore endotracheal tube in the proportions of 1 part oxygen to 2 parts nitrous oxide at a high rate of flow throughout the operation. The blood pressure was allowed to fall to its lowest level during the early stages of the operation, but, if the systolic pressure fell below 40 mm., it was corrected with a small dose of *d*-methylamphetamine (methedrine®) or *l*-arterenol. The liver was inspected for color and tenseness of the capsule, and the surgeon was asked to palpate the organ and to estimate its degree of flaccidity or turgidity. A small quantity of vasopressor drug was then given intravenously. After the systolic pressure had risen to 70 mm. Hg or higher, the liver was again inspected and palpated. In 14 of the 17 patients the liver appeared cyanosed at systolic pressures between 45 and 60 mm. although tissues elsewhere were well oxygenated. In 11 the liver became turgid and rubbery to the touch at systolic pressures between 45 and 60 mm. These changes were reversed when the blood-pressure was raised by methedrine or noradrenaline. Occult liver damage may result from this temporary hypoxia, and the systolic pressure should not be allowed to fall below 60 mm., which was found to be the critical figure for the obvious changes in this series.

2:49-98 (July 12) 1952

Reason and Unreason in Psychological Medicine. E. B. Strauss.—p. 49.
Degeneration of Spinal Cord Associated with Cervical Spondylosis. P. D. Bedford, F. D. Bosanquet and W. R. Russell.—p. 55.
Fractures of Neck of Femur: Simple Technique for Insertion of Smith-Petersen Nail. T. T. Stamm.—p. 59.
Oral Penicillin in Prophylaxis of Streptococcal Infection in Rheumatic Children. A. H. Gale, W. A. Gillespie and C. B. Perry.—p. 61.
Ectopic Pregnancy Inside Uterine Wall in Fibromatous Uterus. L. Achmatowicz.—p. 63.
Outbreak Due to Salmonella Brancaster. E. Hinden, J. Taylor and W. W. Walther.—p. 64.
Loss and Recovery of Sight in Measles Encephalitis. G. H. Jennings.—p. 66.
*"Milk Poisoning" and "Calcium Gout." E. G. McQueen.—p. 67.

"Milk Poisoning" and "Calcium Gout."—McQueen presents the case of a man, aged 56, who had had a duodenal ulcer for a number of years and had been intermittently on an ulcer diet. There were two hard lumps on his left forearm. Radiography showed deposits of opaque material on the radial side of the left wrist. When he was admitted to the hospital in July, 1950, he said that since January, 1950, he had been drinking about a gallon of milk a day. He had continued taking aluminum hydroxide gel (amphojel®) and alkaline powders alternately. He had not noticed the lumps until July, when an extremely painful, tender swelling developed in the wrist and dorsum of his left hand. The swelling disappeared in about a week, but the lumps at the lower end of the radius remained. The same process was repeated at the elbow. In September white chalk-like plaques were found in the sclera of each eye. Radiography revealed gross calcification in several other areas, including the iliac arteries and the radial arteries. Numerous blood studies showed a high level of serum calcium. Treatment consisted in removing all calcium-containing foods from the diet and withholding alkalis except aluminum hydroxide. Belladonna and barbiturates were given to help control his ulcer symptoms. On this regime he improved. The lumps at the wrist and elbow diminished in size. The sequence of events in this case suggest those that the author believes take place in gout: The capacity for holding calcium in soluble form having been exceeded, calcium began to be deposited in insoluble form. In this case, as in uric-acid gout, the deposits gave rise to signs of inflammation. The development of this syndrome may not be possible in the absence of renal disease. Long-continued and excessive consumption of alkalis may be prerequisite for the development of this syndrome and may possibly be responsible for initiating the renal damage. The onset of symptoms dated from the time the patient started drinking an enormous amount of milk. When milk and other calcium-containing foods were removed from his diet, the symptoms and most of the calcium deposits disappeared. Therefore, this may truly be called a case of "milk poisoning."

Lotta Contro Tuberculosi, Rome

22:261-392 (May-June) 1952. **Partial Index**

First Clinical Results of Isonicotinic Acid Hydrazide Therapy in Pulmonary Tuberculosis: Theoretical Concepts and Practical Suggestions. E. Morelli and G. Daddi.—p. 296.
Anatomic and Pathological Changes in Patients Treated with Isonicotinic Acid Hydrazide. C. Pana', N. Belli and A. Perelli.—p. 303.
*Importance and Action of Isonicotinic Acid Hydrazide. F. Ragazzini, A. Masi and M. Giusti.—p. 308.

Isonicotinic Acid Hydrazide in Tuberculous Meningitis.—General or local therapy of tuberculous meningitis with isonicotinic acid hydrazide was carried out in 120 patients who were previously treated with streptomycin, sulfonamides, and *p*-aminosalicylic acid. In systemic therapy an initial dose of 1 to 2 mg. per kilogram of body weight was given orally every eight hours and was gradually increased to 5 mg. per kilogram. When, in a few severe cases, the drug was given intravenously, 2 mg. per kilogram were given in a 1% solution of the drug. In a few other cases the drug was given intramuscularly. No disturbances to the nervous system were observed; constipation occurred in some patients, and others had tremor of the extremities. In local therapy isonicotinic acid hydrazide and streptomycin were injected simultaneously intrathecally or into the cisterna magna. When injected intraspinally, the initial dose was 0.10 mg. per kilogram and was gradually increased to 0.80 mg. This was equal to the streptomycin dose. Only one-half of this dose was given intracisternally. The therapy was well tolerated, and cytochemical examination of the spinal fluid did not reveal great changes. The drug remained in the fluid for a shorter period than streptomycin, especially when the drug was given orally. Combination of local and systemic therapy is thus suggested as a means of obtaining a level of isonicotinic acid hydrazide with a definite antibiotic activity in the spinal fluid. Temperature became normal despite a temporary initial rise in some patients during the first days of therapy. There was a sudden increase in appetite and body weight; the velocity of erythrocyte sedimentation decreased, hemoglobin and red blood cells remained unchanged, the number of leukocytes decreased, and the number of eosinophils increased. The drug had an hypoglycemic effect, and tuberculin allergy was increased. Improvement was quick and pronounced in some patients in poor condition, others were cured, and some in whom cachexia was present survived. Although a definite evaluation is still premature, the authors feel that a combination of isonicotinic acid hydrazide and streptomycin will give good results because in vitro studies revealed a synergistic action of the two drugs.

Medical Journal of Australia, Sydney

1:801-836 (June 14) 1952

Seeds of Time: Impact of Microbiology on Human Affairs Since Lister's Day. M. Burnet.—p. 801.
Dissecting Aortic Aneurysm. S. Milazzo.—p. 807 .
Psychiatric Disorders in General Practice. H. M. Birch.—p. 813.
Short-Acting Muscle Relaxant, Succinyl-Choline-Chloride. R. H. Orton. —p. 817.
Observations on Use of "Scoline" as Muscle Relaxant. J. E. Williams. —p. 818.

1:837-868 (June 21) 1952. **Partial Index**

Urinary Calculus: Notes on Its History and Mode of Formation. E. S. J. King.—p. 837.
Treatment of Ureteric Calculi. G. R. Davidson.—p. 840.
Anatomical and Pathological Considerations in Prostatectomy. D. B. Duffy.—p. 842.
Gram-Negative Bacilli in Urinary Infection. E. W. Kyle.—p. 845.
Chyluria. P. Row.—p. 847.
Scarlet Fever. W. M. Ket.—p. 850.

1:869-904 (June 28) 1952

Dangers of Antibiotics. F. H. Wilson.—p. 869.
Dangers of Antibiotics. E. Thomson.—p. 870.
Observations on Utility of Haemagglutination and Haemolytic Tests in Pulmonary Tuberculosis. T. H. Steel and S. Fisher.—p. 874.
*Treatment of Lead Poisoning by Intravenous Administration of Sodium Thiosulphate. D. O. Shiels.—p. 879.
Superficial Fungous Infection in Victoria. E. S. Mancy.—p. 883.
Administration of Cortisone by Aerosol Method in Treatment of Bronchial Asthma. C. M. Marshall.—p. 884.

Intravenous Sodium Thiosulfate in Lead Poisoning.—Sodium thiosulfate was administered intravenously in doses of 30 grains (1.8 gm.) in a few cubic centimeters of water on alternate days to 18 patients with lead poisoning, 16 of whom were employed in lead mines. The number of injections required to relieve symptoms varied from 2 or 3 to about 12. In the majority the improvement in the patient's clinical condition was rapid, and there were no recurrences. In order to give a numerical estimate of the improvement obtained by the patients, a comparison was made of the ratio of monocytes and large lymphocytes to small lymphocytes before treatment began, and at a short interval afterwards. The average ratio for the 18 patients was 1: 23 before treatment and 3: 22 after some days of treatment. This increase in the ratio of monocytes and large lymphocytes to small lymphocytes is highly significant statistically. That the improvement in clinical condition and in the aforementioned ratio was not due merely to removal from contact with lead at work was shown by the fact that similar rapid clinical improvement occurred in a person who had been away from work for over five months before the treatment was started, as well as in a number of persons with similar but milder symptoms who were treated while still remaining at work under the lead hazards that produced their symptoms.

Minerva Medica, Turin

43:917-948 (May 3) 1952

Treatment of Some Infantile Encephalopathies. F. Negro.—p. 927.
*Treatment of Epidemic Parotitis with *p*-Aminobenzoic Acid, Aureomycin, Chloramphenicol (Chloromycetin®), and Terramycin. G. Racca.—p. 931.

Antibiotics in Epidemic Parotitis.—The therapeutic effects of *p*-aminobenzoic acid, aureomycin, chloramphenicol (chloromycetin®), and terramycin on epidemic parotitis were compared in 75 patients to whom the drugs were given daily in equally divided doses every six hours. Twenty-eight patients received orally 1 to 2 gm. of *p*-aminobenzoic acid, with total doses of from 3 gm. to 38 gm. Twenty patients received orally 1, 2, or 3 gm. of aureomycin, with total doses of from 4 gm. to 18 gm. Twenty-two patients were given orally and sometimes rectally 1, 2, or 3 gm. of chloramphenicol, with total doses of from 4 gm. to 12 gm. Five patients received orally 1 or 1.5 gm. of terramycin. Total doses were 4 gm. to one patient, 5 gm. to another, and 4.5 gm. to the other three. In most patients therapy was begun in the first days of illness and was continued for from 3 to 10 days. None of the drugs was effective in restoring temperature to normal; *p*-aminobenzoic acid had little effect on the swelling of the parotid gland, while the other drugs had none. None influenced the swelling of the submaxillary glands nor the already existing complications to the testes. Chloramphenicol and terramycin were good prophylactics against involvement of the genital organs, whereas the other two drugs had little effect. Aureomycin and chloramphenicol had a beneficial action on secondary meningeal reactions. The only side effects were two instances of slight intolerance to aureomycin.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

96:1573-1628 (June 28) 1952. **Partial Index**

*Skin Bleeding and Necrosis in Patients with Thrombosis Treated with Bishydroxycoumarin. H. Verhagen and M. U. Wiersema.—p. 1578.
Fatal Pulmonary Embolism with Prolonged Course. O. H. Dijkstra. —p. 1585.
*Undesirable Secondary Effects of Administration of BCG. D. P. R. Keizer.—p. 1589.

Hemorrhages and Necrosis of Skin After Treatment with Bishydroxycoumarin.—This paper recounts observations on eight patients who were treated with bishydroxycoumarin or a derivative of that drug on account of thrombophlebitis. Between the fifth and seventh days after onset of treatment, extensive hemorrhages appeared in the skin and the subcutaneous tissue. Subsequently these tissues became necrotic. The authors found no other reports of this complication.

Undesirable Secondary Effects of BCG.—Keizer describes observations on seven young children from 2 months to 2 years old who were treated with BCG. In the first group (four boys and one girl) the BCG was given by mouth. All five of these children had general lymphadenitis, atypical tuberculous infiltrates, scrophuloderma, multiple breakdown of lymph nodes, tracheobronchial lymphadenitis with atelectasis, otitis media, mastoiditis, and peripheral facial paralysis. The two boys of the second group received the BCG by hypodermic injection. They had chronic ulcerations of the skin and early signs of tuberculous lymphadenitis. All these children were strong and well nourished at the time of treatment with BCG. Consequently this treatment cannot be regarded as harmless, although the prognosis as regards survival was favorable. Oral administration seems more dangerous than the intracutaneous method.

Practitioner, London

168:1-110 (July) 1952. **Partial Index**

Clinical Assessment of Cardiac Efficiency. P. D. White.—p. 5.
Treatment of Cardiac Arrhythmias. A. Hunter.—p. 14.
Heart Disease as Cause of Sudden Death. S. Oram.—p. 20.
Surgery of Heart and Great Vessels. T. H. Sellors.—p. 29.
Practical Value of Cardiac Catheterization. J. F. Goodwin.—p. 40.
Heart Disease in Pregnancy. A. M. Jones.—p. 49.
Nicotinamide and Pellagra: Review of Development of Knowledge and of Present Position. L. J. Harris.—p. 57.
Social and Medical Aspects of Tattooing. A. J. Rook and P. J. B. Thomas.—p. 60.

Presse Médicale, Paris

60:981-1000 (June 28) 1952

"Becegitis" and Hamster. P. Haudurov and W. Rosset.—p. 981.
*Experimental Use of "Despecific" Heterologous Plasma in Man. M. Larget, Y. Culot and Debat.—p. 981.
Control of Eosinophilia in Course of Postoperative Disease. M. Nicol and M. Beltan.—p. 983.
Acute Pulmonary Edema and Its Classic Description. R. Lacassie. —p. 985.

Experiments in Man with Despeciated Heterologous Plasma.—Erythrocytes were removed by centrifugation from plasma derived from calves, and the plasma was treated by chemical and physical means to remove its species specificity. This type of plasma then was used for anaphylactic experiments in nine persons. Some of these persons were given an intravenous injection of 500 cc. of this plasma and eight days later an intracutaneous injection of the same plasma. The remaining persons were given an intravenous infusion of 500 cc. of plasma, and later on a second "challenging" infusion of 500 cc. of plasma. Not a single positive intracutaneous reaction was observed in the first group of persons, and not a single undesirable anaphylactic effect was produced by the "challenging" infusion in the other group. The authors then studied the therapeutic action of the plasma on patients in shock, its effect on blood volume and proteinemia, its elimination in the urine, and its effect on

the constituents of the blood as compared with the effects of human plasma under the same conditions. Conclusions drawn from the results obtained were as follows: The despeciated heterologous plasma raises the blood volume. It increases temporarily the proteinemia, and the extent and duration of this increase is the same as that produced by human plasma. It has little effect on the constituents of the blood, except for a mild and temporary diminution of the prothrombin level. It does not cause a true anaphylactic reaction. Occasionally there is slight elimination of albumin in the urine.

60:1021-1036 (July 9) 1952

Recurrent Amyotrophic Encephalitis; Clinical, Electroencephalographic and Electromyographic Findings. T. Alajouanine, J. Nick, J. Lefebvre and J. Scherrer.—p. 1021.
Study of 14 Cases of Insulin Lipodystrophy. R. Boulin, H. Chimènes and R. Tourneur.—p. 1024.
*Theory of "General Adaptation Syndrome"; Its Unreality, Description and Refutation of Selye's Concept. P. Decourt.—p. 1028.

Refutation of General Adaptation Syndrome. — According to Selye's concept, any prolonged stress owing to a specific agent produces nonspecific reactions, which, with respect to this agent, always evolve in three distinct stages: the alarm reaction, the stage of resistance, and the stage of exhaustion. This syndrome has been explained on the basis of an adrenal cortex mechanism. However, the number of experiments carried out by Selye do not suffice for the establishment of a general law. Contrary to Selye's assertion, the evolvement of the specific reaction does not follow a unique pattern, but shows multiple types, differing from that which Selye considers as constant and universal. This can be illustrated in connection with chronic intoxication with arsenic salts, regarded by Selye as the sample-type of the general adaptation syndrome. Animal experiments performed by other workers have demonstrated that a true increase of specific resistance to arsenic salts does not exist. The apparent increase in resistance produced by the repeated oral administration of the insoluble salts is due solely to an inflammatory change in the intestinal mucous membrane, which prevents the organism from absorbing a considerable amount of the damaging agent. The occurrence of such a change in the localized specific resistance in certain tissue zones demonstrates the origin from the tissues rather than the humoral origin of the many changes of the specific resistance to stress. In not a single case does the reaction to arsenical stress correspond to the scheme described by Selye as universal. Three other types of variations in the development of "specific resistance" were demonstrated in connection with morphine and barbituric acid derivatives, tetanus and diphtheria toxins, and peptone, which all were considered by Selye as characteristic agents causing stress. On the basis of many precise biological facts that have been confirmed by other scientists, the author concludes that Selye's general adaptation syndrome does not exist. Concerning the adrenal cortex mechanism, which, according to Selye, explains the increase or diminution of the specific resistance, the author recalls that a nonspecific mechanism cannot account for a "specific" phenomenon. His own observations showed that the variations in the specific resistance are the consequence of multiple mechanisms, among which the local tissue or cell factors play, in general, a primary part.

Revista Médica de Chile, Santiago

80:195-258 (April) 1952. **Partial Index**

Lipoid Metabolism in Human Arteriosclerosis and Its Modification by Potassium Iodide. O. Avendaño, J. Mardones, M. Penna and others.—p. 195.
Distal Nephron Nephrosis or Acute Tubular Disease. R. Ortúzar, G. Letelier and R. Barahona.—p. 200.
*Post-Hepatitis Syndrome. H. Ducci, R. Katz and R. Barahona.—p. 210.
Treatment of Auricular Fibrillation with Quinidine. R. Armas Cruz, F. Rojas Villegas and M. Besoain Santander.—p. 220.

Posthepatitis Syndrome.—Various more or less pronounced subjective and objective disturbances, chiefly dyspepsia, constitute the posthepatitis syndrome, which follows an acute attack of hepatitis in a significant number of cases. Periodic examination of 125 patients with acute hepatitis for a maximum of 20 months showed that 31 had symptoms clearly attributable to the liver disease. Dyspepsia was the principal complaint, accompanied in some cases by hepatomegaly. Objective evidence of disturbed liver function was not regularly obtained; the results of sulfobromophthalein (bromsulfalein®) tests, for example, were normal in all 19 of the patients studied in detail. The objective signs that were found consisted chiefly of an increase in urinary coproporphyrin and histological abnormalities as shown by liver biopsy. The prognosis is variable; certain patients who had had posthepatitis symptoms for as long as six months after the period of jaundice subsequently recovered completely. Patients with residual disturbances following acute hepatitis should be kept under observation for prolonged periods.

Schweizerische medizinische Wochenschrift, Basel

82:677-696 (June 28) 1952. **Partial Index**

Surgical Treatment of Tuberculosis of Lymph Nodes of the Neck. E. K. Oppikofer.—p. 677.
*Treatment of Tuberculous Lymphoma of Neck, with Particular Consideration of Value of Tonsillectomy. O. Hasler and A. Weder.—p. 682.
Effect of Chaulmoogra Oil Alone and Combined with *p*-Aminosalicylic Acid or Amithiozone on Experimental Tuberculosis in Mice. H. Hurni.—p. 685.

Treatment of Tuberculous Lymphoma of Neck.—Of 125 female and 43 male patients with tuberculous lymphoma of the neck who were treated at the Saint Claire Hospital in Basel between 1945 and 1950, 114 submitted to follow-up examinations within 1 to 6 years. As a rule tonsillectomy had been performed on all these patients, and microscopic examination of the removed tonsils revealed tuberculosis of the tonsils in 59 of the 114 patients, while 55 had nonspecific chronic tonsillitis. Of 52 patients whose treatment of the lymphoma consisted of tonsillectomy alone, 22 were cured, 20 were improved to such an extent that they could be considered as cured, and only 10 had recurrences. The therapeutic effect of tonsillectomy alone on the lymphoma was approximately the same in the patients with specific and in the patients with nonspecific chronic tonsillitis. Of the remaining 62 patients who were subjected to tonsillectomy as well as to surgical intervention on the diseased lymph nodes, 44 were cured, 11 were improved, and 7 had recurrences. Of the total of 114 patients, 66 (58%) recovered, 31 (27%) were improved, and only 17 (15%) had recurrences. As a result of these experiences the authors state that tonsillectomy is definitely indicated as first procedure in the treatment of tuberculous lymphoma of the neck. Radical excision of the lymphoma with subsequent roentgen irradiation should be attempted in cases in which the lymphoma does not show any tendency to regress after the tonsillectomy. In cases with progressive formation of abscesses in the involved lymph nodes, incision, excochleation, and local treatment may be sufficient. Chemotherapy without surgical treatment did not prove effective in the presence of foci with poor blood supply, but occasionally streptomycin alone or combined with *p*-aminosalicylic acid before the surgical intervention and for a short time after may be valuable in preventing hematogenous dissemination. Complications such as miliary dissemination or activation of another quiescent tuberculous focus did not occur after the tonsillectomy or after surgical intervention on the lymphoma.

82:717-736 (July 12) 1952. **Partial Index**

*Protective Inoculation Against Influenza; Experience in Personnel of City Hospital in Basel in 1951. A. Bernstein, H. Reber and E. Sheris.—p. 717.
*Night Secretion of Acid Gastric Juice in Healthy Persons and in Patients with Gastrointestinal Diseases. H. Hegglin.—p. 720.
Relationship Between Somatic and Psychic Characteristics of Children. A. Horn.—p. 725.

Protective Inoculation Against Influenza.—At the onset of the influenza epidemic 1950/1951 in Basel, 515 of the 1,100 employees of the City Hospital were inoculated with a vaccine in which the influenza virus strain causing the epidemic had been incorporated. The influenza morbidity was 4.5% among the vaccinated employees, as compared to 8.4% in the nonvaccinated employees. In 168 of the vaccinated persons, the serum content of hemagglutinin-inhibiting antibody to the influenza-virus strains FM_1 and PR_8 was determined. There was an aver-

age increase in antibody of 2.4 times after a single subcutaneous inoculation with 0.4 cc. of vaccine, and an increase of 4.3 times after a one-stage intracutaneous injection of 0.2 cc. of vaccine into each forearm. After a two-stage intracutaneous inoculation, repeating the same dose after an interval of six days, the average antibody level was increased 7.5 times when compared to that before vaccination. Of the subcutaneously vaccinated persons 38% showed a significant rise in antibody titer, as compared to 62% of those subjected to one-stage intracutaneous vaccination and to 79% of those subjected to two-stage intracutaneous vaccination. The antibody titer remained below Salk's critical protective titer of 128 in 55% of the persons who had been subjected to subcutaneous vaccination, in 29% of those subjected to one-stage intracutaneous vaccination, and in 15.5% of those subjected to two-stage intracutaneous vaccination. General undesirable effects of short duration such as mild rise of temperature, fatigue, and pain in joints, were observed in one-fourth of the subcutaneously vaccinated persons and in one-third of those subjected to intracutaneous vaccination. Local reactions such as redness, nodules, and sterile pustules, occurred after the vaccination in 48% of the subcutaneously vaccinated persons, in 85% of those subjected to one-stage intracutaneous vaccination, and in 94% of those with two-stage intracutaneous vaccination. Within five months after the vaccination local reactions to the vaccine, such as red nodules, spots or small scars, still could be demonstrated in 70% of those who had been subjected to one-stage intracutaneous vaccination and in 83% of those subjected to two-stage intracutaneous vaccination. Of the subcutaneously vaccinated, red spots or nodules were still present in 18%.

Night Secretion of Acid Gastric Juice.—At 5:30 p. m., 300 cc. of a watery oatmeal soup and 150 cc. of weak peppermint tea without sugar were given to 25 healthy persons and 58 patients with gastrointestinal disorders. Of the 58 patients, 21 had chronic gastritis, 1 gastric neurosis, 2 gastroduodenitis, 11 gastric ulcer, and 23 duodenal ulcer. At 7 p. m. a duodenal tube was introduced nasally and the stomachs of the 83 persons were aspirated at hourly intervals up to 6 a. m. The fluid obtained was measured, filtered, and titrated. Free acid and total acidity were determined. In all persons secretion of gastric juice and production of acid predominated before midnight and decreased after midnight. The healthy persons showed the lowest incidence (26%) of continuous night secretion. Secretory pauses were equally distributed among the two halves of the night; the anacidity phases occurred most frequently after midnight. During repeated examinations each person maintained the same pattern of secretion. Continuous night secretion of acid gastric juice was observed in 83% of the patients with duodenal ulcer; there was a minimum of secretory pauses and of anacidity periods. Hypersecretion and hyperacidity were observed in some of the patients. Continuous night secretion of acid gastric juice was observed in 55% of the patients with ulcer of the stomach. In the other 45% the duration of secretory pauses and of anacidity periods did not much exceed that of the healthy persons; there was a tendency to hypoacidity and to anacidity. Patients with chronic gastritis held an intermediate position between those with gastric and duodenal ulcer. A causal relationship between chronic gastritis on one side and gastric and duodenal ulcer on the other side seems possible. It was striking that night secretion of acid up to 70 units occurred in four patients with chronic gastritis and in one with gastric ulcer who did not show free acid on fasting or after caffeine. In three of these patients free acid was missing even after administration of histamine. Furthermore in half of the patients in this series higher maximum values of free acid were observed during the night than after administration of caffeine. These observations show that neither caffeine nor histamine are maximum stimulants of acidity, and that anacidity following histamine administration does not prove that there is no free acid. On the other hand cases of this type demonstrate the significance of chronic gastritis and night secretion of acid and pepsin in the formation of an ulcer. These products exert their effect on the inflamed gastric and duodenal wall in the absence of any buffer action, and may thus induce an ulcer.

Thorax, London

7:125-204 (June) 1952

*Tertiary Syphilis of Lung and Its Diagnosis. A. D. Morgan, W. E. Lloyd and C. Price-Thomas.—p. 125.
Four Cases of Diabetes Insipidus and Pulmonary Disease. J. D. Spillane.—p. 134.
Humidification of Air Passages. V. E. Negus.—p. 148.
Massive Haemoptysis From Arterio-Bronchial Fistula in Pulmonary Tuberculosis. M. Berard and J. de Beaujeu.—p. 152.
So-Called Middle Lobe Syndrome. B. Fretheim.—p. 156.
Gastro-Oesophageal Haemorrhage in Hepatic Cirrhosis. H. Butler.—p. 159.
Peptic Ulceration and Perforation of Stomach After Oesophagectomy. V. S. Brookes and J. L. Stafford—p. 167.
Radiographic Technique for Study of Lung Pathology. G. J. Cunningham and J. W. Miller.—p. 170.
Failed Thoracoplasty. R. Grenville-Mathers and H. J. Trenchard.—p. 185.

Tertiary Syphilis of Lung.—Acquired syphilis of the lung is a rare condition, but the diagnostic criteria are so variable that it is difficult to assess the degree of rarity. It has been stated that the diagnosis cannot be made with assurance during life, and is often uncertain at the postmortem examination. The clinical, radiological, and pathological criteria of pulmonary syphilis are discussed in connection with a case of tertiary syphilis of the lung. The authors conclude that the gumma is the only specific histological criterion of tertiary syphilis of the lung. They say that in a patient with a suggestive clinical picture, positive serological tests, and a sputum persistently negative for tubercle bacilli, if the radiological lesion clears decisively under antisyphilitic treatment, there are reasonable grounds for diagnosing pulmonary syphilis. If, as the result of lobectomy or necropsy, typical gummas are demonstrated in the lung, then the diagnosis is virtually certain. As a therapeutic test some investigators have recommended intramuscular injections of bismuth for two or three weeks accompanied by potassium iodide thrice daily and oxophenarsine (mapharsen®) in doses of 0.01 to 0.06 mg. at five-day intervals for 10 to 12 injections. If improvement is satisfactory, treatment should be continued as in other forms of visceral syphilis. In a case recorded in 1947 treatment with penicillin was successful. If the patient fails to respond rapidly, the possibility of neoplasm must be reconsidered, and exploratory thoracotomy or lobectomy may be necessary. If the gummas have permanently damaged the lung, it may be liable to hemorrhage, secondary infection or bronchiectasis, and lobectomy or segmental lobectomy may be advisable.

Ugeskrift for Laeger, Copenhagen

114:837-878 (June 26) 1952

Cortisone Treatment of Hyperplasia of Adrenal Cortex. H. Andersen, C. Hansted and M. Sprechler.—p. 837.
*Erroneous Diagnosis in Idiopathic Hypoparathyroidism. C. Hansted.—p. 840.
Dermatomyositis with Hypertrichosis and Polycystic Ovarian Degeneration. H. Andersen, M. Andreassen and C. Hansted.—p. 844.
Effectivity of Podophyllin in Treatment of Condylomata Acuminata. B. Heilesen.—p. 846.

Erroneous Diagnosis in Idiopathic Hypoparathyroidism.—Hypoparathyroidism is characterized by spasms and increased neuromuscular irritability, lowered serum calcium, increased serum phosphorus and normal serum phosphatase; characteristic changes in eyes and teeth, hair, skin and nails support the diagnosis. Electroencephalographic changes may be seen in hypoparathyroidism with and without epileptic attacks, and the disorder may be accompanied by psychic retardation. In cases with less characteristic symptoms the diagnosis is not always made. Spasms in the first months of life may be due to a transient hypoparathyroidism and infantile tetany in children with rickets may perhaps depend on a relative parathyroid insufficiency. The symptoms, complications, and blood chemistry in pseudohypoparathyroidism resemble those in hypoparathyroidism, but are due to a deficient ability to react to the parathyroid hormone. In the first case described typical idiopathic hypoparathyroidism had been diagnosed as infantile tetany in a girl, aged 2½, with latent rickets. The patient's twin sister, probably a uniovular twin, was well. In the second case idiopathic hypoparathyroidism of 13 years' standing, was present in a 19-year-old sister who had been treated for years for epilepsy. There were typical symptoms, trophic changes in eyes, teeth and bones, and mental and electroencephalographic changes.

BOOK REVIEWS

A Handbook of Operative Surgery: Surgery of the Chest. By Julian Johnson, M.D., D.Sc., Professor of Surgery, School of Medicine and Graduate School of Medicine, University of Pennsylvania, Philadelphia, and Charles K. Kirby, M.D., Assistant Professor of Surgery, School of Medicine, University of Pennsylvania. Cloth. $9. Pp. 387, with 81 illustrations by Edna Hill. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1952.

This short handbook was written primarily for general surgeons and surgical residents who wish to acquaint themselves with the fundamentals of accepted thoracic operations and with tested methods of preoperative and postoperative care. The seasoned thoracic surgeon will find little that is new in this book, but he will enjoy reading it. Many illustrations of operations are well done in line drawings. Each step of the operation is carefully explained in the adjoining text. The author has wisely included only those procedures that have been tried and proved successful over a period of years by many surgeons. This book is a compendium of thoracic surgery well illustrated and concisely written for quick reference. It is recommended for those who wish to begin and those who wish to add to their knowledge of thoracic surgery.

Fisiopatología humana. Por Bruno Günther, professor de fisiología y de fisiopatología, Escuela de medicina. Universidad de Concepción, Chile. Prefacio de B. A. Houssay, Premio Nobel de medicina 1947. Cloth. $8. Pp. 624, with illustrations. Universidad de Concepción, Concepción Chile; [sole agent: Librería médica Walter Blunck, Casilla 4053, Santiago de Chile (S. America)], 1950.

This book is intended for use by the students of the University of Concepción, Chile, as a textbook in physiopathology; however, it is too concise and too much of a summary to fulfill this purpose. On the other hand, it appears ideal for a practitioner who wishes to obtain a wide and practical view of some of the problems of every day practice from the physiological, physiopathological, and clinical aspects.

The author discusses the syndromes in methodical order, starting with signs and symptoms, explaining them from the physiological angle, gradually dealing with the physiopathological aspect, and, in conclusion, giving the whole clinical picture with its interpretations. The manner in which the subjects are discussed is simple, precise, and interesting, making the book enjoyable reading for anyone with enough knowledge to be able to absorb its teaching. There is a bibliography at the end of each of the 11 chapters as well as numerous diagrams and graphs. The book is written in Spanish.

The Lipids: Their Chemistry and Biochemistry. Volume I: Chemistry. By Harry J. Deuel Jr., Dean, Graduate School, and Professor of Biochemistry, University of Southern California, Los Angeles. Cloth. $18.50. Pp. 982, with illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; 2a Southampton Row, London, W.C.1, 1951.

This is the first volume of a proposed two volume series that will deal with the chemistry and biochemistry of lipids. This volume treats exclusively the chemistry of the lipids and lipid-like materials that are present in the animal body or in plants. The author has systematized the book to include much detailed information on the structure, synthesis, and chemical and physical properties of the four main classes of lipids: fatty acids, neutral fats, waxes, and phospholipids and cerebrosides. Other chapters give similar detailed treatment of the lipid-related compounds, the carotenoids, and the vitamins A, D, E, and K. The author has included charts and tables wherever information is adaptable to this style, such as in the cataloguing of certain physical properties of classes of compounds. The text has adequate footnotes with numerous references to the original literature. It includes an author and subject index as well as an index to the plant and animal sources of the lipids mentioned.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

The English Pioneers of Anæsthesia (Beddoes, Davy, and Hickman). By F. F. Cartwright. Cloth. $4.50. Pp. 338, with 19 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; John Wright & Sons, Ltd., 42-44, Triangle West, Bristol 8, England, 1952.

This valuable historical contribution presents many details of the preliminary work that made possible the clinical introduction of anesthesia. It is based on three short biographies of Thomas Beddoes, Humphrey Davy, and Henry Hill Hickman, each of whom made important basic contributions toward the later development of anesthesiology. Dr. Cartwright's publication represents the culmination of 12 years spent in gathering material from numerous sources. Since the author's own family inhabited the same part of England and moved in the same circles as Beddoes and Hickman, he has been able to secure previously unrevealed facts concerning these three scientists that make fascinating reading. He has written in a subtly gracious style and has employed excellent descriptive language. The volume is freely interspersed with interesting quotations and revealing footnotes. Archibald D. Marston, F.R.C.S., dean of the Faculty of Anaesthetics, Royal College of Surgeons, London, wrote the foreword. This book contains 12 chapters, the last being devoted to a "Concluding Essay" in which the author summarizes the relationship of many factors that have been responsible for the development of anesthesia during the past two centuries. A bibliography and an adequate index are included. The illustrations are well selected. This volume emphasizes the fact that anesthesiologists should not overvalue the present achievements in the specialty but should give due consideration to the work that has gone before. This book is recommended to all anesthesiologists and to everyone interested in medical history. It should find a place in all medical school libraries.

Blood Transfusion in Clinical Medicine. By P. L. Mollison, M.D., M.R.C.P., M.R.C.S., Director, Medical Research Council's Blood Transfusion Research Unit. With foreword by Sir Alan N. Drury, C.B.E., F.R.S. Cloth. $8. Pp. 456, with 59 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1951.

This extraordinarily interesting volume on blood transfusion is the work of an authority in this field. As he says, "Within the past twelve years the sum total of new knowledge which has been derived from the practice of blood transfusion has been remarkable. In the United States the discoveries of Landsteiner, Levine, and Wiener laid the foundations for a swift and astonishing expansion of the subject of blood groups." Dr. Mollison has been responsible for many of the recent developments. He has contributed much to both the testing of new preservative solutions and the fundamental research dealing with the storage of red blood cells. The author, since the end of the war, has been director of the Blood Transfusion Research Unit set up by the British Medical Research Council. There are 13 chapters, covering all aspects of blood transfusion.

The bibliography is excellent, and the index is satisfactory. Because of the current interest in blood for our military forces, for civil defense, and for use in civilian hospitals, this volume will be of much value. It is an outstanding contribution to the subject that it covers.

Annual Review of Nuclear Science. Volume I. Committee on Nuclear Science, National Research Council, L. F. Curtis, Chairman. Cloth. $6. Pp. 645, with illustrations. Annual Reviews, Inc., Stanford, California, 1952.

This volume is an auspicious beginning of a series that one may expect, with confidence, to become extremely useful to research workers in the field of nuclear science. The chapters, by different authors, deal with such topics as meson physics, theories of nuclear structure, energy levels in light nuclei, and high energy accelerators. Of the 26 chapters, 4 deal with topics of medical interest, namely, radioisotopes in biochemical and medical

research, stable isotopes in biochemical research, genetic effects of radiation, and biological effects of high energy radiation. The last topic gives the most immediate promise of practical application, as it is concerned with the relation of water and oxygen to the mechanism of radiation injury and thus leads to a consideration of protection and treatment.

The fact that these four chapters cover a total of 838 references to recent publications is at once a revelation of the amount of research that is being done in this field and an indication of the value of these annual reviews to future investigators. The volume maintains the high standards of content, indexing, and format to which users of the other annual reviews have become accustomed.

William Smellie: The Master of British Midwifery. By R. W. Johnstone, C.B.E., M.A., M.D. Cloth. $4. Pp. 139, with 30 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, 1952.

This biography of William Smellie is dedicated to Miles Phillips, who, of all living obstetricians, says the author, knows most about and has entered with sympathy most deeply into the life of William Smellie. The author also acknowledges his indebtedness to Dr. John Glaister's "Doctor William Smellie and His Contemporaries." Dr. Glaister, professor of medical jurisprudence in the University of Glasgow, himself a native of Lanark, did much to counterbalance his town's early neglect of the memory of its greatest son by publishing his biography. However, the erudite but all too voluminous biography by Glaister, published more than 60 years earlier, has been out of print for some time. For this and other reasons, obstetricians and other medical men interested in the history of their art will welcome this comparatively brief but excellent account of Smellie and his work.

Seen in retrospect, Smellie's life is the story of the rise and growth of the science and art of obstetrics from the crude, blundering medieval midwifery. Smellie's great contribution, as evaluated by himself, was "to clear away an immensity of the rubbish and superstition which enveloped the whole theory and practice of midwifery." Smellie's description of the mechanism of labor is undoubtedly his greatest, most fundamental, and most far-reaching contribution to obstetrics. As to the quality of his mind, Dr. Johnstone states that it was not of that superlative degree as to tempt us to the use of that elusive term "genius." His seat among the immortals of medical history, Johnstone believes, was won by the fact that his power of thinking for himself and of cutting through the stifling undergrowth of ancient authority and tradition enabled him as a teacher to mold the thought of his own generation to a degree that determined the course of the development of midwifery for all time. Dr. Johnstone made excellent use of the literary and historical material at his command by presenting an authoritative and balanced evaluation of the life and work of "The Master of British Midwifery." Dr. Johnstone's charming literary style adds much to the enjoyment to be derived from reading this remarkable story of a somewhat neglected immortal.

Industry and Tropical Health: Proceedings of the First Industrial Tropical Health Conference, Sponsored by the Harvard School of Public Health, December 8-10, 1950 at Boston, Massachusetts. Cloth. $10. Pp. 316, with illustrations. Harvard School of Public Health, Cambridge, Mass., 1951.

This book contains papers presented during 12 sessions of a two day meeting for a program arranged to bring together industrial medical, health, and executive officials of 23 industrial organizations located in tropical Africa, tropical America, and the Far and Middle East. The purpose was to exchange their experiences and ideas.

Fifty contributions cover a wide scope of problems concerning the integration of health and manpower interests as an important part of industrial production in the parts of the world represented by the speakers. The 12 sessions were divided as follows: industry and health in the Middle East, industry and health in tropical Africa, industry and health in the Far East, industry and health in tropical America, industry's future in tropical health, the conference dinner, organization of industrial health services, antibiotics in certain tropical diseases, nutrition, current research (Harvard School of Public Health), infectious diseases and problems of control, and industrial health hazards. These subjects were chosen to emphasize the application of the principles and practices of modern preventive industrial medicine to large groups as well as individual persons for occupational health evaluation and maintenance.

The comprehensive coverage emphasizes the need for integrating health activities connected with industrial production and those of the general community. It is clearly indicated that the 23 industries represented in the conference have many problems in common with industrial organizations in all geographic locations; however, etiological factors peculiar to a tropical environment are responsible for unusual experiences in the work situations that require special consideration in both education and practice. The book contains a wealth of information supplied by the actual experiences of the individual conference members.

From this meeting there emerged a permanent organization entitled the Industrial Council for Tropical Health, with headquarters at the Harvard School of Public Health. It is the object of this organization to include corporations with tropical operations and, through correspondence and conferences similar to the one described in these proceedings, to continue to share experiences and knowledge for mutual benefit and for the betterment of working conditions and community living among peoples in tropical regions.

Tuberculosis of Bone and Joint. By G. R. Girdlestone and E. W. Somerville, M.B., F.R.C.S., Orthopaedic Surgeon to Wingfield-Morris Orthopaedic Hospital, Oxford. From Nuffield Orthopaedic Centre. Oxford medical publications. Second edition. Cloth. $8.75. Pp. 314, with 182 illustrations. Oxford University Press, 114 Fifth Ave., New York 11; Amen House, Warwick Sq., London, E.C.4, 1952.

Some of the outstanding sections of the book include material on the general nature of tuberculosis of bones and joints and its possible relation to injury. The authors discuss diagnosis, general treatment, local treatment, and operative treatment. The section on provisional diagnosis is exceptionally good. Regional tuberculosis of bones and joints, including the hip, spine (Pott's paraplegia), knee, sacroiliac, foot and ankle, and upper extremities are discussed. Splints, appliances, plaster of paris, and surgical appliances are described and illustrated in the appendix. There is a good section on measurements required by brace makers, a topic that is too often overlooked.

Tuberculosis may be said to be at the crossroads. We are on the threshold of still greater discoveries in the field of chemotherapeutic agents. The time-tested principles, the bedrock of treatment of tuberculosis of bones and joints, were laid down by Hugh Owen Thomas and Sir Robert Jones. This book deals not so much with the latest inventions, new theories, or experimental work as with a sound basis for treatment that has stood the test of time and on which future advances may be superimposed.

The sources of material are well chosen, and the material is well utilized. The textual revision, improved by experience of 10 years, has in no way altered the fundamental concept. The illustrations are clear and instructive. When the authors write, "We are on the threshold of still greater discoveries," they might be psychic in predicting the use of the nicotinamides.

Girdlestone's background of keen interest and experience coupled with his apprenticeship with Sir Robert Jones and Dame Agnes Hunt taught him that only true principles and reasonable practice can survive. The authors have enlarged on the pathology sections and have added new material to the section on radiology.

They have also revised material on the use of splints and plaster. The death of Girdlestone ended a long career of experience with tuberculosis of bones and joints. Every orthopedic surgeon should be familiar with the contents of this book.

Twixt the Cup and the Lip: Psychological and Socio-Cultural Factors Affecting Food Habits. By Margaret Cussler and Mary L. de Give. Cloth. $3.95. Pp. 262, with 26 illustrations. Twayne Publishers, 42 Broadway, New York 4, 1952.

The socio-economic factors governing the dietary habits of three rural Southern communities are discussed in an interesting manner by the authors of this book. The original field work substantiates the conclusions, which are very much what one would expect to find. It is, perhaps, unfortunate that the many

transcripts of conversations with the inhabitants are relegated to the appendixes, since examples of this nature interspersed in the text would serve to hold the reader's attention. This book can be recommended to professional nutritionists who are interested in food habits and attempts to change them and as interesting background material in food patterns for those not directly associated with the field.

The Genetics of Micro-Organisms. By D. G. Catcheside. Cloth. $4.50. Pp. 223, with 36 illustrations. Pitman Publishing Corporation, 2-6 W. 45th St., New York 19; Sir Isaac Pitman & Sons, Ltd., Pitman House, 39-41 Parker St., Kingsway, London, W.C.2, 1951.

Recent developments in the field of genetics have established the existence of a relationship between the genetic constitution of an organism and its biochemical activities. Students of biochemistry, particularly those interested in growth and metabolism, are, therefore, finding it necessary to equip themselves with a knowledge of genetics. This book has been devised to fill such a need.

Genetic principles are illustrated by means of a study of the fungus Neurospora. Genetic analysis, mutation and gene action, and mutation and adaptation are discussed. Specific examples of the application of genetic methods to the study of the intermediate metabolism of Neurospora are cited. An interesting chapter on the sexual reproductive systems of fungi and algae emphasizes the complicated mechanisms in these organisms. Other chapters contain summaries of our present knowledge of the genetics of yeasts, bacteria, viruses, and protozoa.

The author has succeeded in presenting an abundance of information in compact form. A valuable bibliography containing references to the recent literature is appended.

American Health Directory. By Henry Hatton. Paper. $2.50. Pp. 96. Public Affairs Press, 2153 Florida Ave., Washington 8, D. C., 1952.

This little directory of various foundations and agencies engaged in health and medical activities could be extremely useful if it were not so ineptly compiled. One finds material under heart diseases, cardiovascular diseases, angiology, and arteriosclerosis with the sole "see also" reference from arteriosclerosis to multiple sclerosis. There are also references that lead nowhere; from Krebiozen Foundation the reader is directed to cancer, but cancer, in turn, does not list the foundation. Under the headings safety and psychoanalysis one does not find mention of either the National Safety Council or the institutes for psychoanalysis. Although the heading medical fraternities is used, osteopathic professional fraternities occurs as a separate heading. This booklet should be used with extreme care if other sources of information are not available.

Medical Biographies: The Ailments of Thirty-Three Famous Persons. By Philip Marshall Dale, M.D. Cloth. $4. Pp. 259, with 32 portraits. University of Oklahoma Press, Norman, Oklahoma, 1952.

This book provides a fascinating account of the ailments of a group of famous persons; among them are Christopher Columbus, Samuel Pepys, Napoleon Bonaparte, Walt Whitman, Edgar Allan Poe, Andrew Jackson, Charles Darwin, and Guy de Maupassant. What the author has admirably succeeded in accomplishing is well expressed in his own words: "This work is not a study in vital statistics. Obviously both the causes of disability and the causes of death among famous persons are not different from those affecting the contemporary adult population in general. What I have tried to do is to illuminate a dark corner of legitimate biography in a few select instances, with the light of modern medical understanding." This book offers good reading and is highly recommended.

Das Bronchuscarcinom. Von Doz. Dr. G. Salzer, Doz. Dr. M. Wenzl, Dr. R. H. Jenny und Dr. A. Stangl, Leiterin des Röntgeninstitutes der II. chirurgischen Universitätsklinik in Wien. Mit einem Beitrag von Dr. O. Mayrhofer. Cloth. $18.60. Pp. [242], with 367 illustrations. Springer-Verlag, Mölkerbastei 5, Vienna 1, 1952.

The material in this book has been accurately compiled and adequately discussed. The first 143 pages contain the text and a few explanatory illustrations and roentgenograms. Following this there are 99 pages of 120 roentgenograms that depict the various forms of lung carcinoma. That part of this latter section dealing with the roentgenographic aspects of differential diagnosis is particularly well presented.

The segmental anatomy of the bronchial tree is presented in detail, and its relationship to diagnosis is stressed. Bronchoscopy has been given its proper place of importance as a diagnostic aid. The authors discuss the value of cytological diagnosis in some detail and list the statistical data that they have compiled from the literature; the conflicting figures are self-explanatory.

The therapeutic possibilities are discussed in detail, and some definite opinions are expressed in regard to roentgen therapy. A few illustrations depicting operative steps and surgical technique would probably amplify this section of the text tremendously; such informative material is, unfortunately, conspicuous by its absence. This book is timely, exacting, and worth while. It can be recommended to anyone with a reading knowledge of German who is interested in bronchus carcinoma.

Physiologische Chemie: Ein Lehr- und Handbuch für Ärzte, Biologen und Chemiker. Herausgegeben von B. Flaschenträger, unter Mitwirkung von E. Lehnartz. Hervorgegangen aus dem Lehrbuch der physiologischen Chemie von Olof Hammarsten. Erster Band: Die Stoffe. Bearbeitet von D. Ackermann et al. Cloth. 198 marks. Pp. 1600, with 93 illustrations. Springer-Verlag, Reichpietschufer 20, Berlin W. 35 (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, 1951.

As the subtitle indicates, this work has "arisen from" Hammerstein's "Lehrbuch der Physiologischen Chemie." It retains the features that made the "Lehrbuch" invaluable: chapters by experts in the various fields, careful editing to make the work a unified whole, extensive citations to the original literature, and exhaustive indexes. The three pages of corrections for volume 1, most of them quite minor, show the effort taken to make the work accurate. The work will be in two volumes. The first covers the chemistry of biologically important substances, while the second will cover their roles and transformations in living systems. The contributors to volume 1 are German, Scandinavian, and Swiss biochemists covering such subjects as water, minerals, carbohydrates, fats and lipoids, proteins, purines and pyrimidines, pyrroles, enzymes, and animal poisons. The introductory material (172 pages) grounds the reader in the latest theories of chemical structure and physical chemistry, especially as they relate to biological processes. Both German and foreign literature is covered thoroughly through 1947, and some 1948 references are included. The arrangement, illustrations, printing, and binding seem excellent, and the text fairly easy to read even for one whose German is "rusty."

Chemistry of Carbon Compounds: A Modern Comprehensive Treatise. Edited by E. H. Rodd, A.C.G.I., D.I.C., D.Sc. Volume I, Part A: General Introduction and Aliphatic Compounds. Cloth. $20.70. Pp. 777. Elsevier Press, Inc., 402 Lovett Blvd., Houston 6; 118 Spuistraat, Amsterdam, Netherlands, 1951.

This is the first volume of a proposed five volume series on organic chemistry. It may be regarded as a successor to Richter's "Organic Chemistry," since the general framework of that treatise has been retained and recent advances in organic chemistry and new subject matter have been interwoven with it. The volumes are intended to serve as reference works of intermediate size and not as textbooks. An attempt has been made to make the work as comprehensive as possible by including in the body of the text many references to surveys and review articles. The first volume includes a general introduction and a systematic treatment of the aliphatic compounds. The introduction consists of 11 chapters written by several authorities on such problems as the structure, nomenclature, and quantitative analysis of organic compounds and certain physicochemical aspects of organic chemistry. The major emphasis is on the latter subject and includes such topics as crystallography, light absorption, stereochemistry, and reaction mechanisms. The section on the aliphatic compounds is grouped into 11 chapters on saturated and unsaturated hydrocarbons, their halogen derivatives, the monohydric alcohols, the sulfur, nitrogen, and metal derivatives of the alcohols, aldehydes, and ketones, monocarboxylic acids, glycols, the hydroxy-aldehydes and hydroxy-ketones and diketones. The book also has an adequate index. The series will be a welcome addition to the library of those interested in the chemistry of organic compounds, because of its wide scope and adequate references.

QUERIES AND MINOR NOTES

BLEPHAROSPASM

TO THE EDITOR:—*I would appreciate a discussion of the cause, treatment, and prognosis for blepharospasm in a patient, aged 71, who has had for years a tendency to blink and squint the eyes. She has always been active socially, and now she sits with her eyes closed almost all the time. In response to a request to open the eyes, she shuts them tighter than ever, making contortions of the facial muscles. When there is a loud noise, or there is something she wants to see, she has no trouble opening the lids. Twenty-five years ago most of the thyroid was removed; 2 to 4 grains (0.13 to 0.26 gm.) of thyroid a day keeps the basal metabolic rate about normal. The systolic blood pressure varies from 120 to 220 mm. Hg. The diastolic pressure is 80 mm. Hg. at all times. The patient's weight is 198 lb. (89.8 kg.), 40 lb. (18.1 kg.) less than it was in 1946. She has been dieting strenuously for over two months.*

Ellsworth G. Beers, M.D., Seymour, Mo.

ANSWER.—Bilateral blepharospasm in a 71-year-old patient who has shown "a tendency to blink and squint the eyes for several years" is probably a functional neurosis; that is, it is not caused by irritation of the eyes, by pressure on any division of the seventh nerve, or by disease of the orbicularis muscle. Fortunately, comparatively few persons so afflicted progress to the extreme form of blepharospasm, but manifestly continue the exaggerated blink as a habit spasm. The condition is not a clinical characteristic of any neurological disease but is seen often in hysterical and highly neurotic persons. More commonly, however, it occurs in persons past middle age who are unemotional, calm, sensible, intelligent, and otherwise in good health. The spasms begin as mild twitching of the lids of one or both eyes and increase in frequency and force of muscular contraction. There is no trigger point whereby the spasm can be induced by touching a sensitive spot along the facial nerve, but occasionally the spasm will cease and the eyes open naturally when some such spot is pressed. The spasms are likely to occur spontaneously while crossing a street, meeting an acquaintance unexpectedly, or in attempting to carry on a social conversation.

Between the group of causes associated with pain, in which the blepharospasm may be voluntary or unintentional (the so-called reflex group) and the group associated with emotional and psychic disturbances (the so-called pithiatic group, in which the spasms are at least unintentional), is the group of causes that are "organic" in nature. In these cases, blepharospasm is caused by alterations in the brain or by changes in the trigeminal reflex arc. Among the latter are reported cases of parkinsonism, encephalitis, irritation of the vertebral nerve, amyotrophic lateral sclerosis, Parinaud's syndrome, and other disorders of the nervous system. The type of blepharospasm that gives the least indication of its cause develops from irritation in the central nervous system. It is organic in nature and is known as essential blepharospasm. The blepharospasm is usually bilateral and is more likely to be tonic than clonic, although it may be unilateral, with the spasm varying from tonic to clonic. As a rule the spasms do not occur during sleep and are generally increased when the patient attempts to control them by will or when it would be embarrassing or even dangerous for the eyelids to be kept closed. In most cases recorded in the French and German literature, essential blepharospasm is regarded as a delayed sequela of encephalitis. Some instances of blepharospasm are cited in which other neurological disorders that occur some years after an attack of encephalitis are associated. Presumably the mild inflammation occurring within the central nervous system that is associated with lethargic encephalitis lends credence to this presumption.

It is unusual to find a case of blepharospasm or severe tic of the eyelids that can be classified in one category strictly on the basis of its etiology. Many cases of symptomatic blepharospasm eventually require psychotherapy before a complete cure can be obtained, but it is seldom that a patient is completely cured by psychotherapy alone. Obviously, the treatment for symptomatic blepharospasm in a given case should be directed to the pathological condition present, provided it is possible to determine the significant and irritating factors. Three methods of treatment of essential blepharospasm have been advocated, namely, the injection of alcohol into the facial nerve, neurectomy, and electrocoagulation of the facial nerve. Injection of 80% alcohol, following injection of procaine hydrochloride, into the branches of the seventh nerve gives relief from blepharospasm for a period of six to nine months. Repeated injections give relief for shorter periods of time, until six injections over a period of three to six years have been given, after which no relief is obtained. The logical place to inject the nerve is at the parotid plexus behind the mandible. In severe and protracted cases, the most satisfactory treatment is resection of the palpebral, orbicular, and maxillary branches of the seventh nerve.

DUSTING WITH SULFONAMIDE POWDER

TO THE EDITOR:—*What is the current opinion on the value of dusting sterile sulfonamide powder on the surface of small wounds and abrasions in their first aid treatment. Occasionally, sulfonamide sensitivity reactions are so severe that reevaluation of this questionable procedure seems indicated.*

Willis P. Baker, M.D., Santa Ana, Calif.

ANSWER.—The dusting of sterile sulfonamide powder on the surface of wounds or into deeper wounds is not recommended and such use is now generally abandoned. This applies to first aid treatment as well as definitive treatment. As yet, no agent has been shown to increase the rate of wound healing beyond that obtained under optimum physiological conditions. This latter is achieved as far as the local wound is concerned by thorough but gentle cleansing of the wound, removal of devitalized tissue, protection of the wound, and placing of the injured part at rest. If further prophylaxis against infection is deemed necessary, the use of antibiotics by methods other than local dusting is preferred. Furthermore, sulfa compounds used locally act as foreign bodies; they increase wound exudation and may produce local sensitivity reactions.

VAGINAL BLEEDING IN SIX-YEAR-OLD GIRL

TO THE EDITOR:—*Six months ago, a 6-year-old girl in otherwise perfect health had mild vaginal bleeding for three days. It stopped spontaneously, but four days ago recurred. Results of external examination were normal; the hymen is intact, but there is a definite beginning hair growth on each labium. What course should be pursued for more complete vaginal examination? What glandular treatment, if any, should be used? Could this be an extremely early menstruation or an otherwise precocious sexual development?*

H. G. Pudleiner, M.D., Algoma, Wis.

ANSWER.—The main problem is whether or not this patient has a tumor of the adrenals or ovaries causing precocious development or whether she is undergoing spontaneous precocious development. Careful roentgenographic examination of the adrenals, determination of the 17-ketosteroid and estrogen excretion in the urine, careful examination of the external genitalia, and examination of the uterus rectally are suggested. Stereoroentgenographs of the skull should be made to exclude the possibility of a hypothalamic tumor.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

BLOOD GROUPS

TO THE EDITOR:—*A patient wants to know what exists in the blood that makes it a given blood type. He also wants to know the probable blood types of his offspring for any blood type that the mother of his offspring might have.* *M.D., Iowa.*

ANSWER.—This all inclusive query can be answered only superficially in the limited space available. For fuller details the references cited should be consulted. Morphologically, red cells from all human beings appear to be identical. By serologic methods, however, following the pioneer work of Karl Landsteiner, a vast number of individual differences in their structure have been shown to exist. The red cell surface appears to be studded with structures called agglutinogens, which are identified with the aid of antiserums obtained from human beings or experimental animals. The blood to be typed is tested in succession with a battery of reagents, such as anti-A, anti-B, anti-M, anti-N, and anti-Rh_o. Clumping of the cells indicates the presence of the corresponding blood factor on the cells; failure to clump indicates absence of the blood factor in question. Heredity studies show that certain agglutinogens are related to form systems, such as the A-B-O system, the M-N-S system, and the Rh-Hr system. To date, more than 20 blood factors belonging to eight different systems have been identified. Aside from the fact that the agglutinogens are inherited and are integral parts of the red cell envelope, little is known as to how or why they are formed. Apparently, the blood type to which a person belongs does not affect his health any more than does his eye color. In general, the agglutinogens within a system are inherited by multiple allelic genes, and the blood type of every person can be determined at birth and remains constant throughout his life. Of the various blood group systems, the A-B-O and Rh-Hr systems are medically most important because of the role they play in blood transfusion and in erythroblastosis fetalis.

The precise hereditary nature of the blood groups has led to their medicolegal application in cases of disputed parentage. Tables listing the types possible among the offspring when the types of the parents are known are found in the references below. Blood tests can be used only to exclude the possibility of parentage and not to prove parentage. Judging from the question, it is desired to know what findings exclude paternity in cases in which the mother's blood is not available for examination. At the present stage of knowledge, the combinations that exclude paternity are as follows:

	Putative Father	Child
A-B-O system	AB	O
	O	AB
	A_1B	A_2
	A_2	A_1B
M-N system	M	N
	N	M
Rh-Hr system	rh′ negative	hr′ negative
	hr′ negative	rh′ negative

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LINEA ALBA

TO THE EDITOR:—*Is there any therapy for striae or linea alba in a young woman who is concerned about this condition for cosmetic reasons? A 15-year-old girl desires help on account of striae in the skin of the thigh, which appear to be a consequence of rapid physical development and gain in weight.*

L. M. Lide, M.D., Florence, S. C.

ANSWER.—Unfortunately, treatment for linea alba is unsatisfactory. The application of soothing greasy preparations does no harm and sometimes seems to effect a slight cosmetic improvement.

ACUTE LEUKEMIA

TO THE EDITOR:—*A girl, aged 5, has been pale and somewhat under par for one month and has had no appetite for two weeks. One week ago, several large bruises developed on both legs, and for two days she has had tarry stools. She weighs 36 lb. (16.3 kg.) and is 42 in. (106.7 cm.) tall. Her white blood cell count is 32,000 per cubic millimeter, 80% of the cells being reported as immature. Her red blood cell count is 3,200,000 per cubic millimeter, with a hemoglobin level of 5.3 gm. per 100 cc. A bone marrow smear done by a competent hematologist showed that 98% of the cells are blasts. Since the patient has few complaints and is still quite active, the question arises whether she is a good candidate for some of the new antileukemia drugs.*

Oliver S. Hayward, M.D., New London, N. H.

ANSWER.—Apparently this patient has an acute "blastic" leukemia. A determination should be made of the platelet level, which is probably very low and may explain the hemorrhagic tendency. The treatment of choice is cortisone, which should be given in an initial dose of 150 mg. for two to three days and continued in a dose of 75 mg. per day for about three weeks. Potassium chloride, 1½ to 2 gm. daily (in cherry syrup) should be administered with the cortisone. The patient should be carefully watched for changes in blood pressure and for glycosuria. In about 15 to 20% of cases of acute "blastic" leukemia in children, there may be a transitory complete or almost complete remission; the marrow may become free of blasts, the platelet count may return to normal, and the anemia may disappear. Unfortunately, the remissions are more or less short-lived, and in most instances a relapse occurs that can not be influenced further with cortisone treatment. If no effect is seen after a period of three weeks, it is unlikely that cortisone will be effective at all; in such instances, "aminopterin" (4-aminopteroylglutamic acid) may be tried; it should be given intramuscularly in doses of 1 to 2 mg. per day, with close hematological observation. In some cases, again, a complete remission may ensue, and exceptional cases have been observed in which this treatment was successful in maintaining a remission for more than a year. In this consultant's experience, fewer patients respond to "aminopterin" than to cortisone. A combination of these two drugs may also be tried, but this therapy does not produce particularly startling results. If "aminopterin" causes toxic symptoms (loss of hair and severe aplasia of the marrow), treatment with citrovorum factor may be effective in combating the side-effects. Citrovorum factor removes the toxic effects of "aminopterin" much more rapidly than does folic acid. This has been explained on the basis that "aminopterin" blocks the change of folic acid to citrovorum factor, the latter being the physiologically active factor of cell maturation.

RHABDOMYOSARCOMA

TO THE EDITOR:—*I excised an 8 by 8 cm. tumor of three months duration originating from the soleus muscle and invading the gastrocnemius of a 3-year-old boy. The patient recovered with surprisingly little disability. He is now taking corrective orthopedic exercises and wears a modified shoe to prevent calcaneal tipping. The pathologist had diagnosed the tumor as infantile rhabdomyosarcoma and advised radical local excision, which was done. He stated there was evidence of blood vessel invasion and that the ultimate prognosis was not good. Can you give information on the number of cases reported, treatment, and prognosis?* *M.D., New York.*

ANSWER.—As of April, 1950, 208 proved cases of rhabdomyosarcoma had been reported. Of these, 121 originated in the skeletal muscles (Palumbo, L. T.; Leibovitz, M., and Corcoran, T. E.: Rhabdomyosarcoma of Thigh: Report of Case, *Arch. Surg.* **60**:806 [April] 1950). The five year survival rate reported in the literature is 3.3%. The treatment of choice is wide surgical excision or amputation when necessary. The following are some of the most comprehensive papers on the subject: Stout, A. P.: Rhabdomyosarcoma of Skeletal Muscles, *Ann. Surg.* **123**:447 (March) 1946. De, M. N., and Tribedi, B. P.: Skeletal Muscle Tissue Tumour, *Brit. J. Surg* **28**:17 (July) 1940. Jönsson, G.: Malignant Tumors of Skeletal Muscles, Fasciae, Joint Capsules, Tendon Sheaths and Serous Bursae, *Acta Radiol.* suppl. 36, 1938, pp. 1-304. Rakov, A. I.: *Am. J. Cancer* **30**:455 (July) 1937.

EMOTIONAL REACTION FOLLOWING ELECTRIC SHOCK

To the Editor:—*A young laborer received an electric shock, which evidently went through his body from one hand to the other. He returned to work. His foreman, in attempting to show him that he was needlessly afraid, placed his hands in the same position and was killed by an electric shock. Since then, the patient has been disabled, having an anxiety state with moderate depression and also pains and weakness deep in both arms and along the thoracic spine. The patient's strength appears to be normal (the accident happened two weeks ago); deep reflexes in the upper arm are difficult to elicit and when elicited are feeble; reflexes in the upper abdomen are weaker on the left than on the right. No sensory or other neurological disorders could be found. Would further neurological symptoms be expected in the future?*

R. C. Hubbard, M.D., Elgin, Ill.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—It appears that this patient received no significant injury from the electric shock passing through his body from one hand to the other, since the neurological abnormalities reported on subsequent examination were minimal and of doubtful significance. His complaints seem to be related rather to fear and to the emotional stress engendered by the death of his fellow workman. Probably no further neurological symptoms are to be expected in the future. In cases reported in the literature in which severe electric shock passing through the body resulted in neurological abnormalities not leading to death, the abnormalities have taken the form of disseminated lesions that are at their maximum after the shock, tend to diminish for a time, and then remain stationary. Progressive lesions could scarcely be expected to occur as a result of such damage by the electric current. The mechanism by which electric current produces neurological lesions is not understood.

Answer.—On the basis of the evidence given, it appears that this man has an emotional disorder rather than organic neurological disease. The facts in support of that opinion are that he was able to return to work immediately after receiving the shock, that even now there is no loss of strength, no sensory changes, and no other evidences of neurological disturbance except the diminished tendon reflexes in the arms, and that his principal difficulties at present are his apprehension and depression and some rather diffuse subjective complaints. It is unlikely that other evidences of organic neurological disease will appear in the future.

DIFFICULT PROBLEMS OF HEMOGLOBINOMETRY

To the Editor:—*At a hospital staff meeting a discussion arose concerning the 15 gm. hemoglobin tube and the 17 gm. hemoglobin tube used in the Sahli-Hellige method for determining hemoglobin levels. Which of the two tubes is the more acceptable and the more widely used?*

F. W. Jones, M.D., Newton, N. C.

Answer.—The difficult problems of hemoglobinometry and what hemoglobin level is to be considered "100%" is discussed in textbooks of clinical hematology or clinical pathology. There is an excellent discussion in Ham's "Syllabus of Laboratory Examinations in Clinical Diagnosis" (Cambridge, Mass., Harvard University Press, 1950). From a practical standpoint, it has been found advantageous to consider 15.6 gm. to be 100% and to express all values according to the scale determined by this one. It then has to be realized that the values from 80 to 110% constitute the normal range, and, thus, any standardized instrument can be used for expressing any hemoglobin value in grams as well as in per cent. The best method for determining hemoglobin levels is, of course, photoelectrometry, since it precludes the individual variations of visual colorimetry. When using the Sahli method, the time at which the reading is done after dilution of the blood must be standardized. It is best to obtain a reference value from blood measured in a standardized photoelectric colorimeter and then to standardize the Sahli apparatus against this reading.

PAIN IN TONGUE

To the Editor:—*Eight months ago, symptoms of meningitis, which proved to have a syphilitic basis, developed in a middle-aged woman. She was given 600,000 units of penicillin for 14 consecutive days, and she responded promptly. After 6 months, the spinal fluid was re-tested, and although the test results were greatly improved, they were not normal. The patient was given another similar regimen of penicillin, with no trouble. For the last few weeks she has had severe pain in the left side of her tongue. The tongue itself, the neighboring teeth, and other structures all seem normal, and her general condition is satisfactory. This pain is severe at times, and at other times the patient is reasonably comfortable. A nervous state is developing. I have conferred with neurosurgeons and psychiatrists, and they are not able to help. My feeling is that she has a local neuritis, but I am at a loss as to the proper procedure for her care.*

M.D., Tennessee.

Answer.—With the limited information given regarding both the exact nature of the pain and the results of the neurological examination, it would be impossible to make any diagnosis of this patient's condition. She may have trigeminal neuralgia, a gumma involving the trigeminal nerve or part of it, or some painful condition involving the floor of the mouth. It is entirely possible that this condition should be treated by alcohol injection of the mandibular division of the trigeminal nerve or by section of the trigeminal nerve in back of the ganglion, but that could only be determined by a neurological investigation. It is suggested that the patient be referred to a competent neurological surgeon, of which there are several in your locality.

FECAL FISTULA

To the Editor:—*A 15-year-old boy had an appendectomy 10 months ago. The appendix had ruptured near the base, and a thin serous exudate was present. On the fourth postoperative day, an abscess complicated by the fecal fistula developed at the site of the incision. Since then, fecal material has passed through the fistula daily, although for six months only a small amount has been seen on the dressings. The fistula opening measures 2 to 4 mm. in diameter, and a tube of this diameter can be passed directly downward into the cecum. Throughout this period, the patient has remained in excellent health, gained height and weight, and been active physically, although not allowed to indulge in strenuous competitive sports. Since it has been my impression that fecal fistulas of this origin involving the cecum close spontaneously, I have been waiting for closure to occur. The patient wants to indulge in full scale competitive sports, and the family is desirous of operative intervention. Have I waited long enough for closure? What adjuncts for aiding spontaneous closure can be recommended?*

M.D., Michigan.

Answer.—It is true that most fecal fistulas originating from a perforated appendix close spontaneously. If a fistula has persisted for 10 months and there continues to be a discharge, it would be advisable to open the incision and determine whether the cecum is adherent to the abdominal wall, in which event it could be separated and the perforation in the cecum closed. To insure success in this operation, thorough mobilization of the bowel from the abdominal wall is essential.

ADDICTION TO PAREGORIC

To the Editor:—*Please outline treatment for a paregoric (camphorated opium tincture) addict who consumes one pint (473 ml.) of paregoric in two weeks.*

M.D., Maryland.

Answer.—The amounts of opium in paregoric are so small that true withdrawal symptoms should not be expected in a person who had been consuming only one pint of paregoric every 14 days. Withdrawal treatment, therefore, consists merely of abrupt discontinuation of paregoric. Further treatment should be directed to the physical, if any are present, and psychiatric reasons for the use of the paregoric.

TUBERCULOSIS, NEUROSIS, AND PREGNANCY

To the Editor:—*In* The Journal *Aug. 30, 1952, page 1682, is a query on "Tuberculosis, Neurosis, and Pregnancy," concerning a 32-year-old housewife who wants to have a baby; she has minimal bilateral tuberculosis arrested for over one year and a psychoneurosis of over four years' duration. Both she and her husband are described as intelligent, and the advisability of pregnancy is raised. The inquiry was referred to two consultants.*

The first consultant discusses the inactivity of tuberculosis lesions as defined by the American Trudeau Society of the National Tuberculosis Association, advises that the lesions should be inactive for two years before pregnancy, and concludes that advice in the case in question must necessarily be influenced by the economic and social situation as well as the degree of psychoneurosis involved. The questions of how this is influenced by the degree of psychoneurosis and how the psychoneurosis should be handled or whether it should be handled at all are clearly avoided by the euphemism "as well as by the degree of psychoneurosis involved," as though one could measure it by degrees and then advise as to pregnancy. It stands to reason that the degree of any illness is important, but the advice to the physician making the query is merely that he evaluate the degree of psychoneurosis.

The second consultant clearly grasps the situation as consisting of tuberculosis and an emotional problem that he refers to as "mental instability," which is archaic and extremely obscure terminology. He suggests that surgery might be necessary, feeling this is "almost mandatory in view of the mental history," although the mental history consists of a few words. He then makes several oversimplifications, in contradistinction to the above quotation: "A complete arrest and cure of tuberculosis is now a relatively simple matter with present facilities for treating the disease." Fully cognizant of the importance of the emotional difficulty of the patient, he emphasizes this in concluding and advises proper diet and good mental environment (whatever that might be) for a year or two. He then suggests that if the mental disease is more permanent or hereditary it would be better not to think of pregnancy.

What strikes me in these two answers is the lack of appreciation of the fact that persons with tuberculosis can also be treated for psychiatric disturbances and that, indeed, the "provocation" that the second consultant refers to as a flareup of the disease may have its origin in emotional conflict, with concomitant insomnia and anorexia. The point of the question revolves around the presence of a complicating neurosis in a tuberculosis patient, and it is that factor that calls for an answer, since it is the one that evidently perplexed the questioner. The patient should be referred to a psychiatrist for evaluation for therapy, unless the psychoneurosis can be handled adequately by the physician. The psychosomatic and somatopsychic aspects of tuberculosis are becoming increasingly apparent, and the query calls for an unequivocal statement that this woman's neurosis as well as her tuberculosis needs consideration for therapy, prior to advice about pregnancy.

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REMOVAL OF ACNE SCARS

To the Editor:—*In* The Journal, *April 19, 1952 (page 1458), in Queries and Minor Notes the removal of acne scars is discussed. I have for many years employed superficial scarification of the face for the improvement of acne scars, with excellent results. After the affected area is anesthetized with 1% procaine hydrochloride solution (with or without epinephrine), the skin is scarified with a fine needle or the point of a lancet in a crisscross fashion, until it looks like raw meat. Great care must be taken not to cut deeply. Superficial "scratching" is all that is required. The acne scars themselves offer a definite resistance to the needle and should be broken down into pulp. Blood and serum ooze freely but congeal rapidly and, after drying, form a hard glossy covering. No dressing is necessary except for camouflage. The large scab separates after 8 to 10 days, often in one piece, and leaves a smooth pink skin behind. The application of face powder can then be permitted. After such treatment some of the ruggedness and the irregularities of the acne scars have become smoother, but to obtain a maximum result, four to six such treatments are necessary. There should be an interval of three months between treatments.*

This procedure is neither pleasant nor elegant. To inject the greater part of the face demands a large amount of solution, patience on the part of the physician doing it, and stoicism on the part of the patient. Morphine and other sedatives can make things easier for the patient. I have employed general anesthesia once or twice but found the complete relaxation of the facial muscles a handicap, while the turgid skin after injection of the local anesthetic proves an ideal medium to obtain proper scarification. It often needed some persuasion to get the patients to submit to the first treatment; however, once they had seen the result of the first sitting, they came back for more with great regularity. My most obstinate case was that of a girl of 19 who had eight such treatments spread over two and one-half years. A scarification should leave no marks; if they occur they are evidence of faulty technique. An attempt to improve the appearance of smallpox scars in a similar manner failed utterly; the smoother, regular pits left by smallpox are much less amenable to treatment.

W. Gilges, M.D.
P. O. Balovale,
Northern Rhodesia.

TOURNIQUET FOR SNAKE BITE

To the Editor:—*I wish to take mild exception to an item in Queries and Minor Notes in* The Journal *Aug. 23, 1952, page 1610, in which inquiry was made concerning the technique for the application of a tourniquet for snake bite. The answer stated it is necessary to block merely the lymphatic spread of the venom but that there should be no interference with the venous return.*

My experience in Florida, which has its share of venomous snakes, does not conform to this suggestion. If the snake were always considerate enough to bite only into the lymph space, the answer as given would be correct. Unfortunately, snake fangs occasionally empty directly into a vein; in other cases, the wall of the vein is torn by a glancing blow of the fang, and the venom is deposited to the side of the vein, with a milking action consequently occurring. A bite from a venomous snake is always an emergency, and in my opinion the entire limb should be "isolated" from the rest of the body. The tourniquet should be adjusted to block the venous and lymph channels but should not be tight enough to obstruct arterial inflow. By this means an engorgement and hyperemia of the limb will be produced, which will aid in the removal of the venom by suction, the latter being an integral part of the emergency treatment. It is true that such a limb will soon become painful. For this reason, the tourniquet can be loosened for periods of one minute every half hour. The small amount of venom that enters the body at such times should be relatively well tolerated. In addition to the tourniquet, the usual cruciate incisions around the fang marks, and the suction, it might be advisable to give intramuscularly one of the newer sympathomimetic drugs, such as l-arterenol. Such drugs should not cause the tachycardia that epinephrine would produce and that is obviously undesirable. If these drugs are not available at the time of injury, they can be given later in the hospital. In the meantime, the external application of ice or ice water, as suggested by Dr. Frederick M. Allen, should be used. Naturally, polyvalent antivenom should be used if the bite is from a rattlesnake, a copperhead, or a moccasin. For coral snake bites, which are neurotoxic, cobra antivenom should be used if available.

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